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(54) Title: USE OF MATERIALS HAVING ZINC IONOPHORIC BEHAVIOR

(57) Abstract: Disclosed is a method for delivering excess zinc to eukaryotic cells to inhibit the metabolism of the cell, the method comprising treating the cells with a zinc ionophoric that is capable of delivering a zinc ion across a cellular membrane wherein the minimum inhibitory concentration (MIC) of the zinc ionophoric material is less than about 500 ppm.Further disclosed is a method for delivering excess zinc to eukaryotic cells to inhibit the metabolism of the cell, the method comprising treating the cells with a zinc ionophoric material that is capable of delivering a zinc ion across a cellular membrane wherein the zinc ionophoric material is in combination with a zinc containing material and further wherein there is an increase in an intracellular zinc level by 1.5 fold more than would occur in the absence of the zinc ionophoric material.

USE OF MATERIALS HAVING ZINC IONOPHORIC BEHAVIOR

Field

The present invention relates to methods for delivering excess zinc to eukaryotic cells to inhibit the cell metabolism. The present invention also relates to methods of treating microbial infections on the skin or scalp. The present invention further relates to methods for the treatment of dandruff, and compositions which provide improved anti-dandruff activity.

Background

Various anti-dandruff compositions are commercially available or otherwise known in the shampoo art. These compositions typically comprise detersive surfactants and particulate, crystalline anti-microbial agents dispersed and suspended throughout the composition. Anti-microbial agents used for this purpose include sulfur, selenium sulfide and polyvalent metal salts of pyridinethione. During the shampooing process, these anti-microbial agents deposit on the scalp to provide anti-dandruff activity. Soluble anti-dandruff agents, such as ketoconazole, octopirox, and climbasole are also known in the art.

Polyvalent metal salts of pyrithione (also known as 1-hydroxy-2-pyridinethione; 2-pyridinethiol-1-oxide; 2-pyridinethione; 2-mercaptopyridine-N-oxide; pyridinethione; and pyridinethione-N-oxide) are known to be effective biocidal agents and are widely used as fungicides and bacteriocides in paints and metalworking fluids. Polyvalent metal salts of pyrithione are also used as fungicides and bacteriocides in personal care compositions such as foot powders and anti-dandruff shampoos. The polyvalent metal salts of pyrithione are only sparingly soluble in water and include magnesium pyrithione, barium pyrithione, bismuth pyrithione, strontium pyrithione, zinc pyrithione, cadmium pyrithione, and zirconium pyrithione.

Zinc pyrithione is especially useful as anti-microbial agents in personal care compositions. Zinc pyrithione is known as an anti-dandruff component in shampoos. Synthesis of polyvalent pyrithione salts is described in U.S. Patent No. 2,809,971 to Berstein, et al. Other patents disclosing similar compounds and processes for making them include U.S. Patents Nos. 2,786,847; 3,589,999; 3,590,035; and 3,773,770.

While pyrithione biocides have proven useful for a wide range of applications, the utility of these compounds is limited to the control of select species and strains of fungi

and bacteria. Further, while higher concentrations of pyrithione salts have been observed to control the growth of a wider range of organisms, the useful amount of polyvalent metal salts of pyrithione that can be added to a commercial product is limited by efficacy and economic considerations, and environmental concerns.

Despite the options available, consumers still desire a shampoo which provides superior anti-dandruff efficacy versus currently marketed products. Such a superior efficacy can be difficult to achieve.

For example, it was previously believed that anti-dandruff efficacy could be achieved by "solubilizing" a zinc pyrithione complex in a strong chelating agent. One such approach, disclosed in European Patent Application No. 077,630 to Dixon was to "solubilize" zinc pyrithione in a strong chelating agent in the presence of divalent copper cations. However, the "solubilization" process disclosed in the '630 Application actually results in the break down of the chemical structure of the zinc pyrithione complex. The resulting composition contains a complex of the chelating agent/zinc in solution with free pyrithione ions. The free pyrithione ions are soluble in the composition. The '630 Application discloses that this approach results in a clear product that is physically stable and provides anti-dandruff benefits. Such a composition would fall outside of the current Federal Drug Administration monograph for zinc pyrithione.

Summary

The present invention relates to a method for delivering excess zinc to eukaryotic cells to inhibit the metabolism of the cell, the method comprising treating the cells with a zinc ionophoric material. The present invention further relates to a method for delivering excess zinc to eukaryotic cells to inhibit the metabolism of the cell, the method comprising treating the cells with a zinc ionophoric that is capable of delivering a zinc ion across a cellular membrane wherein the minimum inhibitory concentration (MIC) of the zinc ionophoric material is less than about 500 ppm.

The present invention further relates to a method for delivering excess zinc to eukaryotic cells to inhibit the metabolism of the cell, the method comprising treating the cells with a zinc ionophoric material that is capable of delivering a zinc ion across a cellular membrane wherein the zinc ionophoric material is in combination with a zinc containing material and further wherein there is an increase in an intracellular zinc level by 1.5 fold more than would occur in the absence of the zinc ionophoric material.

These and other features, aspects, and advantages of the present invention will become evident to those skilled in the art from a reading of the present disclosure.

Detailed Description

While the specification concludes with claims which particularly point out and distinctly claim the invention, it is believed the present invention will be better understood from the following description.

It has now surprisingly been found, in accordance with the present invention, that anti-dandruff efficacy can be dramatically increased in topical compositions by the use of materials exhibiting zinc ionophoric behavior. Investigations into the anti-fungal mechanism of zinc pyrithione functions have led to the hypothesis that the Zn^{2+} ion plays a very strong role in the toxicity of zinc pyrithione and pyrithione functions as a delivery vehicle for transporting Zn^{2+} to the fungal cell. This understanding has led to the conclusion that, in general, materials that facilitate the transport of Zn^{2+} to cells will be effective anti-fungals and relevant anti-dandruff technologies; these types of materials are termed materials having zinc ionophoric behavior.

An embodiment of the present invention provides a method for delivering excess zinc to eukaryotic cells to inhibit the cells metabolism by the utilization of materials having zinc ionophoric behavior. Another embodiment of the present invention relates to topical skin and/or hair compositions which provide superior anti-dandruff efficacy. Another embodiment of present invention relates to a method for cleansing the hair and/or skin. It is also an object of the present invention to provide a method for treating athlete's foot, microbial infections, improvement of scalp appearance, fungal infections, diaper dermatitis and candidiasis, tinea capitis, yeast infections, and onchyomycosis. These, and other embodiments, will become readily apparent from the detailed description below.

The present invention can comprise, consist of, or consist essentially of the essential elements and limitations of the invention described herein, as well any of the additional or optional ingredients, components, or limitations described herein.

All percentages, parts and ratios are based upon the total weight of the compositions of the present invention, unless otherwise specified. All such weights as they pertain to listed ingredients are based on the active level and, therefore, do not include carriers or by-products that may be included in commercially available materials.

The components and/or steps, including those which may optionally be added, of the various embodiments of the present invention, are described in detail below.

All documents cited are, in relevant part, incorporated herein by reference; the citation of any document is not to be construed as an admission that it is prior art with respect to the present invention.

All ratios are weight ratios unless specifically stated otherwise.

All temperatures are in degrees Celsius, unless specifically stated otherwise.

Except as otherwise noted, all amounts including quantities, percentages, portions, and proportions, are understood to be modified by the word "about", and amounts are not intended to indicate significant digits.

Except as otherwise noted, the articles "a", "an", and "the" mean "one or more"

Herein, "comprising" means that other steps and other ingredients which do not affect the end result can be added. This term encompasses the terms "consisting of" and "consisting essentially of". The compositions and methods/processes of the present invention can comprise, consist of, and consist essentially of the essential elements and limitations of the invention described herein, as well as any of the additional or optional ingredients, components, steps, or limitations described herein.

Herein, "effective" means an amount of a subject active high enough to provide a significant positive modification of the condition to be treated. An effective amount of the subject active will vary with the particular condition being treated, the severity of the condition, the duration of the treatment, the nature of concurrent treatment, and like factors.

A. Zinc Containing Material

The composition of the present invention includes an effective amount of a zinc containing material. Herein "zinc containing material" or ZCM means a material comprising zinc bound covalently, ionically, or physically by a host material.

Preferred embodiments of the present invention include from 0.001% to 10% of a zinc containing material; more preferably from 0.01% to 5%; more preferably still from 0.1% to 3%.

Examples of zinc containing materials useful in certain embodiments of the present invention include the following:

Inorganic Materials: Zinc aluminate, Zinc carbonate, Zinc oxide and materials containing zinc oxide (i.e., calamine), Zinc phosphates (i.e., orthophosphate and pyrophosphate), Zinc selenide, Zinc sulfide, Zinc silicates (i.e., ortho- and meta-zinc silicates), Zinc silicofluoride, Zinc Borate, Zinc hydroxide and hydroxy sulfate, zinc-containing layered materials and combinations thereof.

Further, layered structures are those with crystal growth primarily occurring in two dimensions. It is conventional to describe layer structures as not only those in which all the atoms are incorporated in well-defined layers, but also those in which there are ions or molecules between the layers, called gallery ions (A.F. Wells "Structural Inorganic Chemistry" Clarendon Press, 1975). Zinc-containing layered materials (ZLM's) may have zinc incorporated in the layers and/or as more labile components of the gallery ions.

Many ZLM's occur naturally as minerals. Common examples include hydrozincite (zinc carbonate hydroxide), basic zinc carbonate, aurichalcite (zinc copper carbonate hydroxide), rosasite (copper zinc carbonate hydroxide) and many related minerals that are zinc-containing. Natural ZLM's can also occur wherein anionic layer species such as clay-type minerals (e.g., phyllosilicates) contain ion-exchanged zinc gallery ions. All of these natural materials can also be obtained synthetically or formed in situ in a composition or during a production process.

Another common class of ZLM's, which are often, but not always, synthetic, is layered doubly hydroxides, which are generally represented by the formula $[M^{2+}_{1-x}M^{3+}_{x}(OH)_2]^{x+}\ A^{m-}_{x/m}\cdot nH_2O$ and some or all of the divalent ions (M^{2+}) would be represented as zinc ions (Crepaldi, EL, Pava, PC, Tronto, J, Valim, JB *J. Colloid Interfac. Sci.* **2002**, *248*, 429-42).

Yet another class of ZLM's can be prepared called hydroxy double salts (Morioka, H., Tagaya, H., Karasu, M, Kadokawa, J, Chiba, K *Inorg. Chem.* **1999**, *38*, 4211-6). Hydroxy double salts can be represented by the general formula $[M^{2+}_{1-x}M^{2+}_{1+x}(OH)_{3(1-y)}]^{+}\ A^{n-}_{(1=3y)/n}\cdot nH_2O$ where the two metal ion may be different; if they are the same and represented by zinc, the formula simplifies to $[Zn_{1+x}(OH)_2]^{2x+}\ 2x\ A^{-}\cdot nH_2O$. This latter formula represents (where x=0.4) common materials such as zinc hydroxychloride and zinc hydroxynitrate. These are related to hydrozincite as well wherein a divalent anion replace the monovalent anion. These materials can also be formed in situ in a composition or in or during a production process.

These classes of ZLM's represent relatively common examples of the general category and are not intended to be limiting as to the broader scope of materials which fit this definition.

Natural Zinc containing materials / Ores and Minerals: Sphalerite (zinc blende), Wurtzite, Smithsonite, Franklinite, Zincite, Willemite, Troostite, Hemimorphite and combinations thereof.

Organic Salts: Zinc fatty acid salts (i.e., caproate, laurate, oleate, stearate, etc.), Zinc salts of alkyl sulfonic acids, Zinc naphthenate, Zinc tartrate, Zinc tannate, Zinc phytate, Zinc monoglycerolate, Zinc allantoinate, Zinc urate, Zinc amino acid salts (i.e., methionate, phenylalinate, tryptophanate, cysteinate, etc) and combinations thereof.

Polymeric Salts: Zinc polycarboxylates (i.e., polyacrylate), Zinc polysulfate and combinations thereof.

Physically Adsorbed Forms: Zinc-loaded ion exchange resins, Zinc adsorbed on particle surfaces, Composite particles in which zinc salts are incorporated, (i.e thereof., as core/shell or aggregate morphologies) and combinations

Zinc Salts: zinc acetate, zinc chloride, zinc sulfate, zinc citrate, zinc fluoride, zinc iodide, zinc lactate, zinc oxalate, zinc propionate, zinc salicylate, zinc tannate, zinc tartrate, zinc valerate, zinc gluconate, zinc oxide, zinc carbonate, zinc hydroxide, zinc oleate, zinc phosphate, zinc selenate, zinc silicate, zinc stearate, zinc sulfide, zinc undecylate, and the like, and mixtures thereof; preferably zinc oxide.

Commercially available sources of zinc oxide include Z-Cote and Z-Cote HPI (BASF), and USP I and USP II (Zinc Corporation of America).

Commercially available sources of zinc carbonate include Zinc Carbonate Basic (Cater Chemicals: Bensenville, IL, USA), Zinc Carbonate (Shepherd Chemicals: Norwood, OH, USA), Zinc Carbonate (CPS Union Corp.: New York, NY, USA), Zinc Carbonate (Elementis Pigments: Durham, UK), and Zinc Carbonate AC (Bruggemann Chemical: Newtown Square, PA, USA).

B. Zinc Ionophoric Material (ZIM)

In another embodiment of the present invention, the composition further includes a zinc ionophoric material. Herein, "zinc ionophoric material" and "ZIM" means a material which is a hydrophobic molecule capable of increasing cell permeability to zinc ions (i.e., exhibiting zinc ionophoric behavior). Without being bound by theory, it is believed that ZIMs shield the charge of the zinc ion to be transported, enabling it to penetrate the hydrophobic interior of the lipid bilayer. ZIMs may be channel-forming ionophores or mobile ion carriers. ZIMs may be those commonly known as zinc ionophores or those that are hydrophobic zinc chelators that possess zinc ionophoric behavior. Hydrophobic zinc chelators are materials that bind zinc and increase

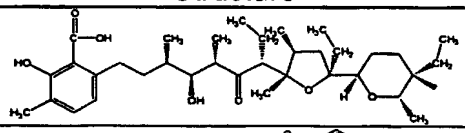
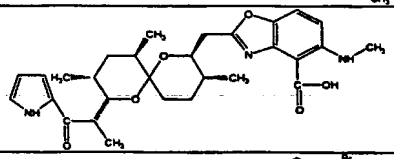
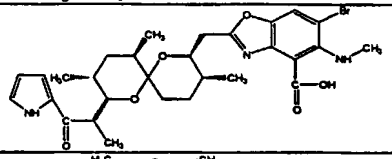
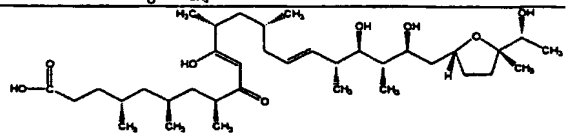
hydrophobicity of zinc ions such that, for example, it will partition into non-aqueous solvents. ZIMs can be effective including zinc being present in the composition or zinc being available within the system wherein a ZIM is present, yet preferred ZIMs contain zinc ions; i.e, zinc salt forms of materials exhibiting zinc ionophoric behavior.

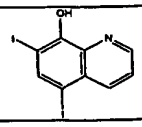
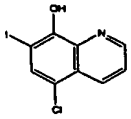
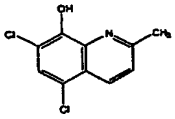
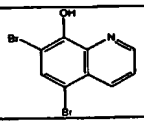
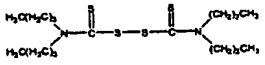
Preferred embodiments include from 0.01% to 5% of a ZIM; more preferably from 0.1% to 2%.

In embodiments having a zinc containing material and a ZIM, the ratio of zinc containing material to ZIM is preferably from 5:100 to 5:1; more preferably from about 2:10 to 3:1; more preferably still from 1:2 to 2:1.

In preferred embodiments of the present invention, the ZIM has a potency against target microorganisms such that the minimum inhibitory concentration ("MIC") is below 5000 parts per million. The MIC is a measurement well understood by those skilled in the art and is indicative of anti-fungal efficacy. Generally, the lower the value of the composition, the better its anti-fungal efficacy, due to increased inherent ability of the anti-dandruff agent to inhibit the growth of microorganisms. The lowest tested dilution of anti-microbial active that yields no growth is defined as the MIC.

Examples of ZIMs useful in embodiments of the present invention include the following:

Class	Name (Synonyms)	Structure
Bio-molecules, Peptides and Naturally Occurring Materials and derivatives thereof having zinc ionophoric behavior	Lasalocid (X537A)	
	A23187 (Calcimycin)	
	4-Br A23187	
	Ionomycin	
	Cyclosporin A	· Cyclic undecapeptide: cyclo-(MeBMT-Abu-Sar-MeLeu-Val-MeLeu-Ala-D-Ala-MeLeu-MeLeu-MeVal)

Hydroxyquinolines	Diodoquin (Iodoquinol; 5,7-Diiodo-8-hydroxyquinoline)	
	Enterovioform (Iodochloro hydroxyquinoline; 5-Cl, 7-I- 8-hydroxyquinoline)	
	Sterosan (Chloroquinaldol; 2-Me, 5,7-Dichloro-8-hydroxyquinoline)	
	5-7-Bibromo-8-hydroxyquinoline	
Sulfur-Based Compounds	Tetra-n-butyl thiuram Disulfide (TBTDS)	
Transport Enhancers	Albumin, histidine, arachidonic acid, picolinic acid, dihydroxyvitamin D_3, ethylmaltol	

In a preferred embodiment, the ZIM is pyrithione or a polyvalent metal salt of pyrithione. Any form of polyvalent metal pyrithione salts may be used, including platelet and needle structures. Preferred salts for use herein include those formed from the polyvalent metals magnesium, barium, bismuth, strontium, copper, zinc, cadmium, zirconium and mixtures thereof, more preferably zinc. Even more preferred for use herein is the zinc salt of 1-hydroxy-2-pyridinethione (known as "zinc pyrithione" or "ZPT"); more preferably ZPT in platelet particle form, wherein the particles have an average size of up to about 20μm, preferably up to about 5μm, more preferably up to about 2.5μm.

Pyridinethione anti-microbial and anti-dandruff agents are described, for example, in U.S. Pat. No. 2,809,971; U.S. Pat. No. 3,236,733; U.S. Pat. No. 3,753,196;

U.S. Pat. No. 3,761,418; U.S. Pat. No. 4,345,080; U.S. Pat. No. 4,323,683; U.S. Pat. No. 4,379,753; and U.S. Pat. No. 4,470,982.

It is further contemplated that when ZPT is used as the anti-microbial particulate in the anti-microbial compositions herein, that an additional benefit of hair growth or re-growth may be stimulated or regulated, or both, or that hair loss may be reduced or inhibited, or that hair may appear thicker or fuller.

Zinc pyrithione may be made by reacting 1-hydroxy-2-pyridinethione (i.e., pyrithione acid) or a soluble salt thereof with a zinc salt (e.g. zinc sulfate) to form a zinc pyrithione precipitate, as illustrated in U.S. Patent No. 2,809,971.

C. Topical Carrier

In a preferred embodiment, the composition of the present invention is in the form of a topical compositions, which includes a topical carrier. Preferably, the topical carrier is selected from a broad range of traditional personal care carriers depending on the type of composition to be formed. By suitable selections of compatible carriers, it is contemplated that such a composition is prepared in the form of daily skin or hair products including skin lotions or hair rinses, daily hair-grooming products, such as hair lotions, hair sprays, hair tonics, conditioning treatments, gels, mousses and dressings, and the like, or they may be prepared in the form of cleansing products, such as hair and/or scalp shampoos, body washes, hand cleansers, water-less hand sanitizer/cleansers, and the like.

Preferably, the topical carrier is water, a common organic solvent, or mixtures thereof. Suitable common organic solvents are C_2-C_3 lower monohydric or polyhydric alcohols such as ethanol, propanol, isopropanol, glycerine, dimethylformamide, dimethylacetamide, and dimethylsulfoxide.

In a preferred embodiment, the carrier is water. Preferably the compositions of the present invention comprise from 40% to 95% water by weight of the composition; preferably from 50% to 85%, more preferably still from 60% to 80%.

In another embodiment of the present invention, the composition is in the form of a solid powder for application to the skin. Such a powder may comprise a solid cosmetic carrier. The solid cosmetic carrier may be talc, which is a hydrated magnesium silicate, used in the form of particles generally less than 40 μm in size; micas, which are aluminosilicates compositions, which exist in the form of scales which are 2 to 200 μm; modified or unmodified starch, in particular rice starch; silica; alumina; boron nitride;

kaolin, which is a hydrated aluminum silicate; zinc and titanium oxides; precipitated calcium carbonate; magnesium carbonate or hydrocarbonate; metallic soaps derived from a carboxylic organic acid having 8 to 22 carbon atoms, for example zinc, magnesium or lithium stearate, zinc laurate, magnesium myristate and the like; synthetic polymer (or copolymer) powders chosen from polyethylene and its derivatives, for example polytetrafluoroethylene, polystyrene and the like; polyacrylates, polymethacrylates, polyesters or polyamides and the like, for example nylon powders; and powders in the form of hollow microspheres made from thermoplastic synthetic material, whose hollow part contains a gas.

All documents cited are, in relevant part, incorporated herein by reference; the citation of any document is not to be construed as an admission that it is prior art with respect to the present invention.

All percentages are by weight of total composition unless specifically stated otherwise.

D. Detersive Surfactant

The composition of the present invention includes a detersive surfactant. The detersive surfactant component is included to provide cleaning performance to the composition. The detersive surfactant component in turn comprises anionic detersive surfactant, zwitterionic or amphoteric detersive surfactant, or a combination thereof. Such surfactants should be physically and chemically compatible with the essential components described herein, or should not otherwise unduly impair product stability, aesthetics or performance.

Suitable anionic detersive surfactant components for use in the composition herein include those which are known for use in hair care or other personal care cleansing compositions. The concentration of the anionic surfactant component in the composition should be sufficient to provide the desired cleaning and lather performance, and generally range from about 5% to about 50%, preferably from about 8% to about 30%, more preferably from about 10% to about 25%, even more preferably from about 12% to about 22%.

Preferred anionic surfactants suitable for use in the compositions are the alkyl and alkyl ether sulfates. These materials have the respective formulae $ROSO_3M$ and $RO(C_2H_4O)_xSO_3M$, wherein R is alkyl or alkenyl of from about 8 to about 18 carbon atoms, x is an integer having a value of from 1 to 10, and M is a cation such as

ammonium, alkanolamines, such as triethanolamine, monovalent metals, such as sodium and potassium, and polyvalent metal cations, such as magnesium, and calcium.

Preferably, R has from about 8 to about 18 carbon atoms, more preferably from about 10 to about 16 carbon atoms, even more preferably from about 12 to about 14 carbon atoms, in both the alkyl and alkyl ether sulfates. The alkyl ether sulfates are typically made as condensation products of ethylene oxide and monohydric alcohols having from about 8 to about 24 carbon atoms. The alcohols can be synthetic or they can be derived from fats, e.g., coconut oil, palm kernel oil, tallow. Lauryl alcohol and straight chain alcohols derived from coconut oil or palm kernel oil are preferred. Such alcohols are reacted with between about 0 and about 10, preferably from about 2 to about 5, more preferably about 3, molar proportions of ethylene oxide, and the resulting mixture of molecular species having, for example, an average of 3 moles of ethylene oxide per mole of alcohol, is sulfated and neutralized.

Other suitable anionic detersive surfactants are the water-soluble salts of organic, sulfuric acid reaction products conforming to the formula [R^1-SO_3-M] where R^1 is a straight or branched chain, saturated, aliphatic hydrocarbon radical having from about 8 to about 24, preferably about 10 to about 18, carbon atoms; and M is a cation described hereinbefore.

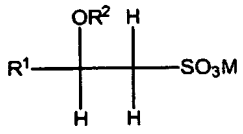
Still other suitable anionic detersive surfactants are the reaction products of fatty acids esterified with isethionic acid and neutralized with sodium hydroxide where, for example, the fatty acids are derived from coconut oil or palm kernel oil; sodium or potassium salts of fatty acid amides of methyl tauride in which the fatty acids, for example, are derived from coconut oil or palm kernel oil. Other similar anionic surfactants are described in U.S. Pat. Nos. 2,486,921; 2,486,922; and 2,396,278.

Other anionic detersive surfactants suitable for use in the compositions are the succinnates, examples of which include disodium N-octadecylsulfosuccinnate; disodium lauryl sulfosuccinate; diammonium lauryl sulfosuccinate; tetrasodium N-(1,2-dicarboxyethyl)-N-octadecylsulfosuccinnate; diamyl ester of sodium sulfosuccinic acid; dihexyl ester of sodium sulfosuccinic acid; and dioctyl esters of sodium sulfosuccinic acid.

Other suitable anionic detersive surfactants include olefin sulfonates having about 10 to about 24 carbon atoms. In addition to the true alkene sulfonates and a proportion of hydroxy-alkanesulfonates, the olefin sulfonates can contain minor amounts

of other materials, such as alkene disulfonates depending upon the reaction conditions, proportion of reactants, the nature of the starting olefins and impurities in the olefin stock and side reactions during the sulfonation process. A non limiting example of such an alpha-olefin sulfonate mixture is described in U.S. Patent 3,332,880.

Another class of anionic detersive surfactants suitable for use in the compositions are the beta-alkyloxy alkane sulfonates. These surfactants conform to the formula



where R^1 is a straight chain alkyl group having from about 6 to about 20 carbon atoms, R^2 is a lower alkyl group having from about 1 to about 3 carbon atoms, preferably 1 carbon atom, and M is a water-soluble cation as described hereinbefore.

Preferred anionic detersive surfactants for use in the compositions include ammonium lauryl sulfate, ammonium laureth sulfate, triethylamine lauryl sulfate, triethylamine laureth sulfate, triethanolamine lauryl sulfate, triethanolamine laureth sulfate, monoethanolamine lauryl sulfate, monoethanolamine laureth sulfate, diethanolamine lauryl sulfate, diethanolamine laureth sulfate, lauric monoglyceride sodium sulfate, sodium lauryl sulfate, sodium laureth sulfate, potassium lauryl sulfate, potassium laureth sulfate, sodium lauryl sarcosinate, sodium lauroyl sarcosinate, lauryl sarcosine, cocoyl sarcosine, ammonium cocoyl sulfate, ammonium lauroyl sulfate, sodium cocoyl sulfate, sodium lauroyl sulfate, potassium cocoyl sulfate, potassium lauryl sulfate, triethanolamine lauryl sulfate, triethanolamine lauryl sulfate, monoethanolamine cocoyl sulfate, monoethanolamine lauryl sulfate, sodium tridecyl benzene sulfonate, sodium dodecyl benzene sulfonate, sodium cocoyl isethionate and combinations thereof.

Suitable amphoteric or zwitterionic detersive surfactants for use in the composition herein include those which are known for use in hair care or other personal care cleansing. Concentration of such amphoteric detersive surfactants preferably ranges from about 0.5% to about 20%, preferably from about 1% to about 10%. Non limiting examples of suitable zwitterionic or amphoteric surfactants are described in U.S. Pat. Nos. 5,104,646 (Bolich Jr. et al.), 5,106,609 (Bolich Jr. et al.).

Amphoteric detersive surfactants suitable for use in the composition are well

known in the art, and include those surfactants broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be straight or branched chain and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic group such as carboxy, sulfonate, sulfate, phosphate, or phosphonate. Preferred amphoteric detersive surfactants for use in the present invention include cocoamphoacetate, cocoamphodiacetate, lauroamphoacetate, lauroamphodiacetate, and mixtures thereof.

Zwitterionic detersive surfactants suitable for use in the composition are well known in the art, and include those surfactants broadly described as derivatives of aliphatic quaternary ammonium, phosphonium, and sulfonium compounds, in which the aliphatic radicals can be straight or branched chain, and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic group such as carboxy, sulfonate, sulfate, phosphate or phosphonate. Zwitterionics such as betaines are preferred.

The compositions of the present invention may further comprise additional surfactants for use in combination with the anionic detersive surfactant component described hereinbefore. Suitable optional surfactants include nonionic and cationic surfactants. Any such surfactant known in the art for use in hair or personal care products may be used, provided that the optional additional surfactant is also chemically and physically compatible with the essential components of the composition, or does not otherwise unduly impair product performance, aesthetics or stability. The concentration of the optional additional surfactants in the composition may vary with the cleansing or lather performance desired, the optional surfactant selected, the desired product concentration, the presence of other components in the composition, and other factors well known in the art.

Non limiting examples of other anionic, zwitterionic, amphoteric or optional additional surfactants suitable for use in the compositions are described in McCutcheon's, Emulsifiers and Detergents, 1989 Annual, published by M. C. Publishing Co., and U.S. Pat. Nos. 3,929,678, 2,658,072; 2,438,091; 2,528,378.

E. Dispersed Particles

The composition of the present invention may include dispersed particles. In the compositions of the present invention, it is preferable to incorporate at least 0.025% by weight of the dispersed particles, more preferably at least 0.05%, still more preferably at least 0.1%, even more preferably at least 0.25%, and yet more preferably at least 0.5%

by weight of the dispersed particles. In the compositions of the present invention, it is preferable to incorporate no more than about 20% by weight of the dispersed particles, more preferably no more than about 10%, still more preferably no more than 5%, even more preferably no more than 3%, and yet more preferably no more than 2% by weight of the dispersed particles.

F. Aqueous Carrier

The compositions of the present invention are typically in the form of pourable liquids (under ambient conditions). The compositions will therefore typically comprise an aqueous carrier, which is present at a level of from about 20% to about 95%, preferably from about 60% to about 85%. The aqueous carrier may comprise water, or a miscible mixture of water and organic solvent, but preferably comprises water with minimal or no significant concentrations of organic solvent, except as otherwise incidentally incorporated into the composition as minor ingredients of other essential or optional components.

G. Additional Components

The compositions of the present invention may further comprise one or more optional components known for use in hair care or personal care products, provided that the optional components are physically and chemically compatible with the essential components described herein, or do not otherwise unduly impair product stability, aesthetics or performance. Individual concentrations of such optional components may range from about 0.001% to about 10%.

Non-limiting examples of optional components for use in the composition include cationic polymers, conditioning agents (hydrocarbon oils, fatty esters, silicones), anti dandruff agents, suspending agents, viscosity modifiers, dyes, nonvolatile solvents or diluents (water soluble and insoluble), pearlescent aids, foam boosters, additional surfactants or nonionic cosurfactants, pediculocides, pH adjusting agents, perfumes, preservatives, chelants, proteins, skin active agents, sunscreens, UV absorbers, vitamins, minerals, herbal/fruit/food extracts, sphingolipids derivatives or synthetical derivative, and clay.

1. Cationic Polymers

The compositions of the present invention may contain a cationic polymer. Concentrations of the cationic polymer in the composition typically range from about 0.05% to about 3%, preferably from about 0.075% to about 2.0%, more preferably from

about 0.1% to about 1.0%. Preferred cationic polymers will have cationic charge densities of at least about 0.9 meq/gm, preferably at least about 1.2 meq/gm, more preferably at least about 1.5 meq/gm, but also preferably less than about 7 meq/gm, more preferably less than about 5 meq/gm, at the pH of intended use of the composition, which pH will generally range from about pH 3 to about pH 9, preferably between about pH 4 and about pH 8. Herein, "cationic charge density" of a polymer refers to the ratio of the number of positive charges on the polymer to the molecular weight of the polymer. The average molecular weight of such suitable cationic polymers will generally be between about 10,000 and 10 million, preferably between about 50,000 and about 5 million, more preferably between about 100,000 and about 3 million.

Suitable cationic polymers for use in the compositions of the present invention contain cationic nitrogen-containing moieties such as quaternary ammonium or cationic protonated amino moieties. The cationic protonated amines can be primary, secondary, or tertiary amines (preferably secondary or tertiary), depending upon the particular species and the selected pH of the composition. Any anionic counterions can be used in association with the cationic polymers so long as the polymers remain soluble in water, in the composition, or in a coacervate phase of the composition, and so long as the counterions are physically and chemically compatible with the essential components of the composition or do not otherwise unduly impair product performance, stability or aesthetics. Non limiting examples of such counterions include halides (e.g., chloride, fluoride, bromide, iodide), sulfate and methylsulfate.

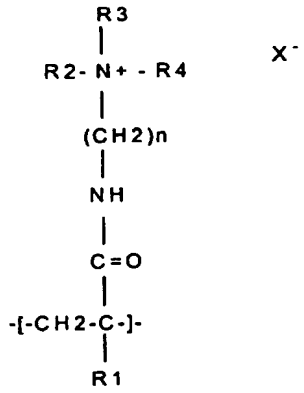
Non limiting examples of such polymers are described in the CTFA Cosmetic Ingredient Dictionary, 3rd edition, edited by Estrin, Crosley, and Haynes, (The Cosmetic, Toiletry, and Fragrance Association, Inc., Washington, D.C. (1982)).

Non limiting examples of suitable cationic polymers include copolymers of vinyl monomers having cationic protonated amine or quaternary ammonium functionalities with water soluble spacer monomers such as acrylamide, methacrylamide, alkyl and dialkyl acrylamides, alkyl and dialkyl methacrylamides, alkyl acrylate, alkyl methacrylate, vinyl caprolactone or vinyl pyrrolidone.

Suitable cationic protonated amino and quaternary ammonium monomers, for inclusion in the cationic polymers of the composition herein, include vinyl compounds substituted with dialkylaminoalkyl acrylate, dialkylaminoalkyl methacrylate, monoalkylaminoalkyl acrylate, monoalkylaminoalkyl methacrylate, trialkyl methacryloxyalkyl ammonium salt, trialkyl acryloxyalkyl ammonium salt, diallyl

quaternary ammonium salts, and vinyl quaternary ammonium monomers having cyclic cationic nitrogen-containing rings such as pyridinium, imidazolium, and quaternized pyrrolidone, e.g., alkyl vinyl imidazolium, alkyl vinyl pyridinium, alkyl vinyl pyrrolidone salts.

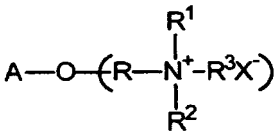
Other suitable cationic polymers for use in the compositions include copolymers of 1-vinyl-2-pyrrolidone and 1-vinyl-3-methylimidazolium salt (e.g., chloride salt) (referred to in the industry by the Cosmetic, Toiletry, and Fragrance Association, "CTFA", as Polyquaternium-16); copolymers of 1-vinyl-2-pyrrolidone and dimethylaminoethyl methacrylate (referred to in the industry by CTFA as Polyquaternium-11); cationic diallyl quaternary ammonium-containing polymers, including, for example, dimethyldiallylammonium chloride homopolymer, copolymers of acrylamide and dimethyldiallylammonium chloride (referred to in the industry by CTFA as Polyquaternium 6 and Polyquaternium 7, respectively); amphoteric copolymers of acrylic acid including copolymers of acrylic acid and dimethyldiallylammonium chloride (referred to in the industry by CTFA as Polyquaternium 22), terpolymers of acrylic acid with dimethyldiallylammonium chloride and acrylamide (referred to in the industry by CTFA as Polyquaternium 39), and terpolymers of acrylic acid with methacrylamidopropyl trimethylammonium chloride and methylacrylate (referred to in the industry by CTFA as Polyquaternium 47). Preferred cationic substituted monomers are the cationic substituted dialkylaminoalkyl acrylamides, dialkylaminoalkyl methacrylamides, and combinations thereof. These preferred monomers conform the to the formula



wherein R^1 is hydrogen, methyl or ethyl; each of R^2, R^3 and R^4 are independently hydrogen or a short chain alkyl having from about 1 to about 8 carbon atoms, preferably from about 1 to about 5 carbon atoms, more preferably from about 1 to about 2 carbon atoms; n is an integer having a value of from about 1 to about 8, preferably from about 1

to about 4; and X is a counterion. The nitrogen attached to R^2, R^3 and R^4 may be a protonated amine (primary, secondary or tertiary), but is preferably a quaternary ammonium wherein each of R^2, R^3 and R^4 are alkyl groups a non limiting example of which is polymethyacrylamidopropyl trimonium chloride, available under the trade name Polycare 133, from Rhone-Poulenc, Cranberry, N.J., U.S.A.

Other suitable cationic polymers for use in the composition include polysaccharide polymers, such as cationic cellulose derivatives and cationic starch derivatives. Suitable cationic polysaccharide polymers include those which conform to the formula



wherein A is an anhydroglucose residual group, such as a starch or cellulose anhydroglucose residual; R is an alkylene oxyalkylene, polyoxyalkylene, or hydroxyalkylene group, or combination thereof; R1, R2, and R3 independently are alkyl, aryl, alkylaryl, arylalkyl, alkoxyalkyl, or alkoxyaryl groups, each group containing up to about 18 carbon atoms, and the total number of carbon atoms for each cationic moiety (i.e., the sum of carbon atoms in R1, R2 and R3) preferably being about 20 or less; and X is an anionic counterion as described in hereinbefore.

Preferred cationic cellulose polymers are salts of hydroxyethyl cellulose reacted with trimethyl ammonium substituted epoxide, referred to in the industry (CTFA) as Polyquaternium 10 and available from Amerchol Corp. (Edison, N.J., USA) in their Polymer LR, JR, and KG series of polymers. Other suitable types of cationic cellulose includes the polymeric quaternary ammonium salts of hydroxyethyl cellulose reacted with lauryl dimethyl ammonium-substituted epoxide referred to in the industry (CTFA) as Polyquaternium 24. These materials are available from Amerchol Corp. under the tradename Polymer LM-200.

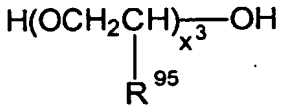
Other suitable cationic polymers include cationic guar gum derivatives, such as guar hydroxypropyltrimonium chloride, specific examples of which include the Jaguar series commercially avaialable from Rhone-Poulenc Incorporated and the N-Hance series commercially available from Aqualon Division of Hercules, Inc. Other suitable cationic polymers include quaternary nitrogen-containing cellulose ethers, some examples of which are described in U.S. Pat. No. 3,962,418. Other suitable cationic

polymers include copolymers of etherified cellulose, guar and starch, some examples of which are described in U.S. Pat. No. 3,958,581. When used, the cationic polymers herein are either soluble in the composition or are soluble in a complex coacervate phase in the composition formed by the cationic polymer and the anionic, amphoteric and/or zwitterionic detersive surfactant component described hereinbefore. Complex coacervates of the cationic polymer can also be formed with other charged materials in the composition.

Techniques for analysis of formation of complex coacervates are known in the art. For example, microscopic analyses of the compositions, at any chosen stage of dilution, can be utilized to identify whether a coacervate phase has formed. Such coacervate phase will be identifiable as an additional emulsified phase in the composition. The use of dyes can aid in distinguishing the coacervate phase from other insoluble phases dispersed in the composition.

2. Nonionic polymers

Polyalkylene glycols having a molecular weight of more than about 1000 are useful herein. Useful are those having the following general formula:



wherein R^{95} is selected from the group consisting of H, methyl, and mixtures thereof. Polyethylene glycol polymers useful herein are PEG-2M (also known as Polyox WSR® N-10, which is available from Union Carbide and as PEG-2,000); PEG-5M (also known as Polyox WSR® N-35 and Polyox WSR® N-80, available from Union Carbide and as PEG-5,000 and Polyethylene Glycol 300,000); PEG-7M (also known as Polyox WSR® N-750 available from Union Carbide); PEG-9M (also known as Polyox WSR® N-3333 available from Union Carbide); and PEG-14 M (also known as Polyox WSR® N-3000 available from Union Carbide).

3. Conditioning agents

Conditioning agents include any material which is used to give a particular conditioning benefit to hair and/or skin. In hair treatment compositions, suitable

conditioning agents are those which deliver one or more benefits relating to shine, softness, combability, antistatic properties, wet-handling, damage, manageability, body, and greasiness. The conditioning agents useful in the compositions of the present invention typically comprise a water insoluble, water dispersible, non-volatile, liquid that forms emulsified, liquid particles. Suitable conditioning agents for use in the composition are those conditioning agents characterized generally as silicones (e.g., silicone oils, cationic silicones, silicone gums, high refractive silicones, and silicone resins), organic conditioning oils (e.g., hydrocarbon oils, polyolefins, and fatty esters) or combinations thereof, or those conditioning agents which otherwise form liquid, dispersed particles in the aqueous surfactant matrix herein. Such conditioning agents should be physically and chemically compatible with the essential components of the composition, and should not otherwise unduly impair product stability, aesthetics or performance.

The concentration of the conditioning agent in the composition should be sufficient to provide the desired conditioning benefits, and as will be apparent to one of ordinary skill in the art. Such concentration can vary with the conditioning agent, the conditioning performance desired, the average size of the conditioning agent particles, the type and concentration of other components, and other like factors.

1. Silicones

The conditioning agent of the compositions of the present invention is preferably an insoluble silicone conditioning agent. The silicone conditioning agent particles may comprise volatile silicone, non-volatile silicone, or combinations thereof. Preferred are non-volatile silicone conditioning agents. If volatile silicones are present, it will typically be incidental to their use as a solvent or carrier for commercially available forms of non-volatile silicone materials ingredients, such as silicone gums and resins. The silicone conditioning agent particles may comprise a silicone fluid conditioning agent and may also comprise other ingredients, such as a silicone resin to improve silicone fluid deposition efficiency or enhance glossiness of the hair.

The concentration of the silicone conditioning agent typically ranges from about 0.01% to about 10%, preferably from about 0.1% to about 8%, more preferably from about 0.1% to about 5%, more preferably from about 0.2% to about 3%. Non-limiting examples of suitable silicone conditioning agents, and optional suspending agents for the silicone, are described in U.S. Reissue Pat. No. 34,584, U.S. Pat. No. 5,104,646, and U.S. Pat. No. 5,106,609. The silicone conditioning agents for use in the

compositions of the present invention preferably have a viscosity, as measured at 25°C, from about 20 to about 2,000,000 centistokes ("csk"), more preferably from about 1,000 to about 1,800,000 csk, even more preferably from about 50,000 to about 1,500,000 csk, more preferably from about 100,000 to about 1,500,000 csk.

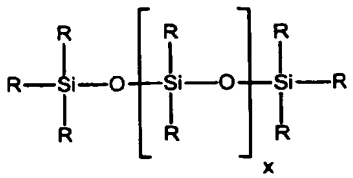
The dispersed silicone conditioning agent particles typically have a number average particle diameter ranging from about 0.01μm to about 50μm. For small particle application to hair, the number average particle diameters typically range from about 0.01μm to about 4μm, preferably from about 0.01μm to about 2μm, more preferably from about 0.01μm to about 0.5μm. For larger particle application to hair, the number average particle diameters typically range from about 4μm to about 50μm, preferably from about 6μm to about 30μm, more preferably from about 9μm to about 20μm, more preferably from about 12μm to about 18μm.

Background material on silicones including sections discussing silicone fluids, gums, and resins, as well as manufacture of silicones, are found in *Encyclopedia of Polymer Science and Engineering*, vol. 15, 2d ed., pp 204-308, John Wiley & Sons, Inc. (1989).

a. Silicone oils

Silicone fluids include silicone oils, which are flowable silicone materials having a viscosity, as measured at 25°C, less than 1,000,000 csk, preferably from about 5 csk to about 1,000,000 csk, more preferably from about 100 csk to about 600,000 csk. Suitable silicone oils for use in the compositions of the present invention include polyalkyl siloxanes, polyaryl siloxanes, polyalkylaryl siloxanes, polyether siloxane copolymers, and mixtures thereof. Other insoluble, non-volatile silicone fluids having hair conditioning properties may also be used.

Silicone oils include polyalkyl or polyaryl siloxanes which conform to the following Formula (III):



wherein R is aliphatic, preferably alkyl or alkenyl, or aryl, R can be substituted or unsubstituted, and x is an integer from 1 to about 8,000. Suitable R groups for use in

the compositions of the present invention include, but are not limited to: alkoxy, aryloxy, alkaryl, arylalkyl, arylalkenyl, alkamino, and ether-substituted, hydroxyl-substituted, and halogen-substituted aliphatic and aryl groups. Suitable R groups also include cationic amines and quaternary ammonium groups.

Preferred alkyl and alkenyl substituents are C_1 to C_5 alkyls and alkenyls, more preferably from C_1 to C_4, more preferably from C_1 to C_2. The aliphatic portions of other alkyl-, alkenyl-, or alkynyl-containing groups (such as alkoxy, alkaryl, and alkamino) can be straight or branched chains, and are preferably from C_1 to C_5, more preferably from C_1 to C_4, even more preferably from C_1 to C_3, more preferably from C_1 to C_2. As discussed above, the R substituents can also contain amino functionalities (e.g. alkamino groups), which can be primary, secondary or tertiary amines or quaternary ammonium. These include mono-, di- and tri- alkylamino and alkoxyamino groups, wherein the aliphatic portion chain length is preferably as described herein.

b. Amino and Cationic silicones

Cationic silicone fluids suitable for use in the compositions of the present invention include, but are not limited to, those which conform to the general formula (V):

$$(R_1)_aG_{3-a}\text{-Si-}(\text{-OSiG}_2)_n\text{-}(\text{-OSiG}_b(R_1)_{2-b})_m\text{-O-SiG}_{3-a}(R_1)_a$$

wherein G is hydrogen, phenyl, hydroxy, or C_1-C_8 alkyl, preferably methyl; a is 0 or an integer having a value from 1 to 3, preferably 0; b is 0 or 1, preferably 1; n is a number from 0 to 1,999, preferably from 49 to 499; m is an integer from 1 to 2,000, preferably from 1 to 10; the sum of n and m is a number from 1 to 2,000, preferably from 50 to 500; R_1 is a monovalent radical conforming to the general formula $CqH_{2q}L$, wherein q is an integer having a value from 2 to 8 and L is selected from the following groups:

$$\text{-N}(R_2)\text{CH}_2\text{-CH}_2\text{-N}(R_2)_2$$

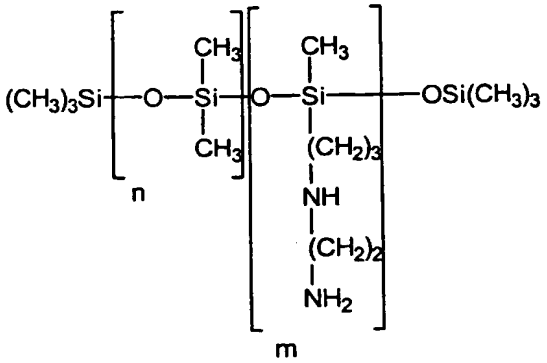
$$\text{-N}(R_2)_2$$

$$\text{-N}(R_2)_3A^-$$

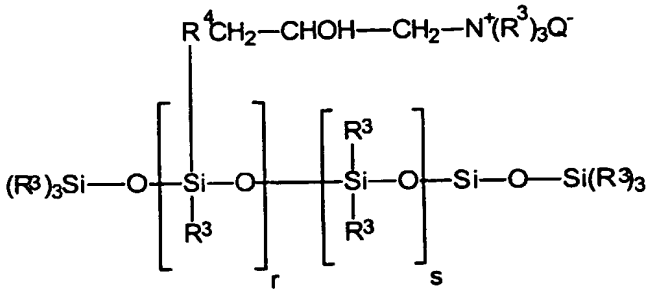
$$\text{-N}(R_2)\text{CH}_2\text{-CH}_2\text{-NR}_2H_2A^-$$

wherein R_2 is hydrogen, phenyl, benzyl, or a saturated hydrocarbon radical, preferably an alkyl radical from about C_1 to about C_{20}, and A^- is a halide ion.

An especially preferred cationic silicone corresponding to formula (V) is the polymer known as "trimethylsilylamodimethicone", which is shown below in formula (VI):



Other silicone cationic polymers which may be used in the compositions of the present invention are represented by the general formula (VII):



wherein R^3 is a monovalent hydrocarbon radical from C_1 to C_{18}, preferably an alkyl or alkenyl radical, such as methyl; R_4 is a hydrocarbon radical, preferably a C_1 to C_{18} alkylene radical or a C_{10} to C_{18} alkyleneoxy radical, more preferably a C_1 to C_8 alkyleneoxy radical; Q^- is a halide ion, preferably chloride; r is an average statistical value from 2 to 20, preferably from 2 to 8; s is an average statistical value from 20 to 200, preferably from 20 to 50. A preferred polymer of this class is known as UCARE SILICONE ALE 56™, available from Union Carbide.

c. Silicone gums

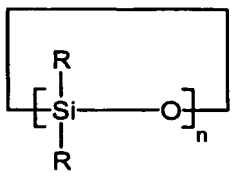
Other silicone fluids suitable for use in the compositions of the present invention are the insoluble silicone gums. These gums are polyorganosiloxane materials having a viscosity, as measured at 25°C, of greater than or equal to 1,000,000 csk. Silicone gums are described in U.S. Pat. No. 4,152,416; Noll and Walter, *Chemistry and*

Technology of Silicones, New York: Academic Press (1968); and in General Electric Silicone Rubber Product Data Sheets SE 30, SE 33, SE 54 and SE 76. Specific non-limiting examples of silicone gums for use in the compositions of the present invention include polydimethylsiloxane, (polydimethylsiloxane) (methylvinylsiloxane) copolymer, poly(dimethylsiloxane) (diphenyl siloxane)(methylvinylsiloxane) copolymer and mixtures thereof.

d. High refractive index silicones

Other non-volatile, insoluble silicone fluid conditioning agents that are suitable for use in the compositions of the present invention are those known as "high refractive index silicones," having a refractive index of at least about 1.46, preferably at least about 1.48, more preferably at least about 1.52, more preferably at least about 1.55. The refractive index of the polysiloxane fluid will generally be less than about 1.70, typically less than about 1.60. In this context, polysiloxane "fluid" includes oils as well as gums.

The high refractive index polysiloxane fluid includes those represented by general Formula (III) above, as well as cyclic polysiloxanes such as those represented by Formula (VIII) below:



wherein R is as defined above, and n is a number from about 3 to about 7, preferably from about 3 to about 5.

The high refractive index polysiloxane fluids contain an amount of aryl-containing R substituents sufficient to increase the refractive index to the desired level, which is described herein. Additionally, R and n must be selected so that the material is non-volatile.

Aryl-containing substituents include those which contain alicyclic and heterocyclic five and six member aryl rings and those which contain fused five or six member rings. The aryl rings themselves can be substituted or unsubstituted.

Generally, the high refractive index polysiloxane fluids will have a degree of

aryl-containing substituents of at least about 15%, preferably at least about 20%, more preferably at least about 25%, even more preferably at least about 35%, more preferably at least about 50%. Typically, the degree of aryl substitution will be less than about 90%, more generally less than about 85%, preferably from about 55% to about 80%.

Preferred high refractive index polysiloxane fluids have a combination of phenyl or phenyl derivative substituents (more preferably phenyl), with alkyl substituents, preferably C_1-C_4 alkyl (more preferably methyl), hydroxy, or C_1-C_4 alkylamino (especially $-R^1NHR^2NH2$ wherein each R^1 and R^2 independently is a C_1-C_3 alkyl, alkenyl, and/or alkoxy).

When high refractive index silicones are used in the compositions of the present invention, they are preferably used in solution with a spreading agent, such as a silicone resin or a surfactant, to reduce the surface tension by a sufficient amount to enhance spreading and thereby enhance the glossiness (subsequent to drying) of hair treated with the compositions.

Silicone fluids suitable for use in the compositions of the present invention are disclosed in U.S. Pat. No. 2,826,551, U.S. Pat. No. 3,964,500, U.S. Pat. No. 4,364,837, British Pat. No. 849,433, and *Silicon Compounds*, Petrarch Systems, Inc. (1984).

e. Silicone resins

Silicone resins may be included in the silicone conditioning agent of the compositions of the present invention. These resins are highly cross-linked polymeric siloxane systems. The cross-linking is introduced through the incorporation of trifunctional and tetrafunctional silanes with monofunctional or difunctional, or both, silanes during manufacture of the silicone resin.

Silicone materials and silicone resins in particular, can conveniently be identified according to a shorthand nomenclature system known to those of ordinary skill in the art as "MDTQ" nomenclature. Under this system, the silicone is described according to presence of various siloxane monomer units which make up the silicone. Briefly, the symbol M denotes the monofunctional unit $(CH_3)_3SiO_{0.5}$; D denotes the difunctional unit $(CH_3)_2SiO$; T denotes the trifunctional unit $(CH_3)SiO_{1.5}$; and Q denotes the quadra- or tetra-functional unit SiO_2. Primes of the unit symbols (e.g. M', D', T', and Q') denote substituents other than methyl, and must be specifically defined for each occurrence.

Preferred silicone resins for use in the compositions of the present invention include, but are not limited to MQ, MT, MTQ, MDT and MDTQ resins. Methyl is a

preferred silicone substituent. Especially preferred silicone resins are MQ resins, wherein the M:Q ratio is from about 0.5:1.0 to about 1.5:1.0 and the average molecular weight of the silicone resin is from about 1000 to about 10,000.

The weight ratio of the non-volatile silicone fluid, having refractive index below 1.46, to the silicone resin component, when used, is preferably from about 4:1 to about 400:1, more preferably from about 9:1 to about 200:1, more preferably from about 19:1 to about 100:1, particularly when the silicone fluid component is a polydimethylsiloxane fluid or a mixture of polydimethylsiloxane fluid and polydimethylsiloxane gum as described herein. Insofar as the silicone resin forms a part of the same phase in the compositions hereof as the silicone fluid, i.e. the conditioning active, the sum of the fluid and resin should be included in determining the level of silicone conditioning agent in the composition.

2. Organic conditioning oils

The conditioning component of the compositions of the present invention may also comprise from about 0.05% to about 3%, preferably from about 0.08% to about 1.5%, more preferably from about 0.1% to about 1%, of at least one organic conditioning oil as the conditioning agent, either alone or in combination with other conditioning agents, such as the silicones (described herein).

a. Hydrocarbon oils

Suitable organic conditioning oils for use as conditioning agents in the compositions of the present invention include, but are not limited to, hydrocarbon oils having at least about 10 carbon atoms, such as cyclic hydrocarbons, straight chain aliphatic hydrocarbons (saturated or unsaturated), and branched chain aliphatic hydrocarbons (saturated or unsaturated), including polymers and mixtures thereof. Straight chain hydrocarbon oils preferably are from about C_{12} to about C_{19}. Branched chain hydrocarbon oils, including hydrocarbon polymers, typically will contain more than 19 carbon atoms.

Specific non-limiting examples of these hydrocarbon oils include paraffin oil, mineral oil, saturated and unsaturated dodecane, saturated and unsaturated tridecane, saturated and unsaturated tetradecane, saturated and unsaturated pentadecane, saturated and unsaturated hexadecane, polybutene, polydecene, and mixtures thereof. Branched-chain isomers of these compounds, as well as of higher chain length hydrocarbons, can also be used, examples of which include highly branched, saturated or unsaturated, alkanes such as the permethyl-substituted isomers, e.g., the permethyl-

substituted isomers of hexadecane and eicosane, such as 2, 2, 4, 4, 6, 6, 8, 8-dimethyl-10-methylundecane and 2, 2, 4, 4, 6, 6-dimethyl-8-methylnonane, available from Permethyl Corporation. Hydrocarbon polymers such as polybutene and polydecene. A preferred hydrocarbon polymer is polybutene, such as the copolymer of isobutylene and butene. A commercially available material of this type is L-14 polybutene from Amoco Chemical Corporation. The concentration of such hydrocarbon oils in the composition preferably range from about 0.05% to about 20%, more preferably from about 0.08% to about 1.5%, and even more preferably from about 0.1% to about 1%.

b. Polyolefins

Organic conditioning oils for use in the compositions of the present invention can also include liquid polyolefins, more preferably liquid poly-α-olefins, more preferably hydrogenated liquid poly-α-olefins. Polyolefins for use herein are prepared by polymerization of C_4 to about C_{14} olefenic monomers, preferably from about C_6 to about C_{12}.

Non-limiting examples of olefenic monomers for use in preparing the polyolefin liquids herein include ethylene, propylene, 1-butene, 1-pentene, 1-hexene, 1-octene, 1-decene, 1-dodecene, 1-tetradecene, branched chain isomers such as 4-methyl-1-pentene, and mixtures thereof. Also suitable for preparing the polyolefin liquids are olefin-containing refinery feedstocks or effluents. Preferred hydrogenated α-olefin monomers include, but are not limited to: 1-hexene to 1-hexadecenes, 1-octene to 1-tetradecene, and mixtures thereof.

c. Fatty Esters

Other suitable organic conditioning oils for use as the conditioning agent in the compositions of the present invention include, but are not limited to, fatty esters having at least 10 carbon atoms. These fatty esters include esters with hydrocarbyl chains derived from fatty acids or alcohols (e.g. mono-esters, polyhydric alcohol esters, and di- and tri-carboxylic acid esters). The hydrocarbyl radicals of the fatty esters hereof may include or have covalently bonded thereto other compatible functionalities, such as amides and alkoxy moieties (e.g., ethoxy or ether linkages, etc.).

Specific examples of preferred fatty esters include, but are not limited to: isopropyl isostearate, hexyl laurate, isohexyl laurate, isohexyl palmitate, isopropyl palmitate, decyl oleate, isodecyl oleate, hexadecyl stearate, decyl stearate, isopropyl isostearate, dihexyldecyl adipate, lauryl lactate, myristyl lactate, cetyl lactate, oleyl stearate, oleyl

oleate, oleyl myristate, lauryl acetate, cetyl propionate, and oleyl adipate.

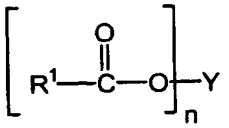
Other fatty esters suitable for use in the compositions of the present invention are mono-carboxylic acid esters of the general formula R'COOR, wherein R' and R are alkyl or alkenyl radicals, and the sum of carbon atoms in R' and R is at least 10, preferably at least 22.

Still other fatty esters suitable for use in the compositions of the present invention are di- and tri-alkyl and alkenyl esters of carboxylic acids, such as esters of C_4 to C_8 dicarboxylic acids (e.g. C_1 to C_{22} esters, preferably C_1 to C_6, of succinic acid, glutaric acid, and adipic acid). Specific non-limiting examples of di- and tri- alkyl and alkenyl esters of carboxylic acids include isocetyl stearyol stearate, diisopropyl adipate, and tristearyl citrate.

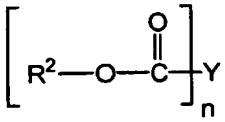
Other fatty esters suitable for use in the compositions of the present invention are those known as polyhydric alcohol esters. Such polyhydric alcohol esters include alkylene glycol esters, such as ethylene glycol mono and di-fatty acid esters, diethylene glycol mono- and di-fatty acid esters, polyethylene glycol mono- and di-fatty acid esters, propylene glycol mono- and di-fatty acid esters, polypropylene glycol monooleate, polypropylene glycol 2000 monostearate, ethoxylated propylene glycol monostearate, glyceryl mono- and di-fatty acid esters, polyglycerol poly-fatty acid esters, ethoxylated glyceryl monostearate, 1,3-butylene glycol monostearate, 1,3-butylene glycol distearate, polyoxyethylene polyol fatty acid ester, sorbitan fatty acid esters, and polyoxyethylene sorbitan fatty acid esters.

Still other fatty esters suitable for use in the compositions of the present invention are glycerides, including, but not limited to, mono-, di-, and tri-glycerides, preferably di- and tri-glycerides, more preferably triglycerides. For use in the compositions described herein, the glycerides are preferably the mono-, di-, and tri-esters of glycerol and long chain carboxylic acids, such as C_{10} to C_{22} carboxylic acids. A variety of these types of materials can be obtained from vegetable and animal fats and oils, such as castor oil, safflower oil, cottonseed oil, corn oil, olive oil, cod liver oil, almond oil, avocado oil, palm oil, sesame oil, lanolin and soybean oil. Synthetic oils include, but are not limited to, triolein and tristearin glyceryl dilaurate.

Other fatty esters suitable for use in the compositions of the present invention are water insoluble synthetic fatty esters. Some preferred synthetic esters conform to the general Formula (IX):



wherein R^1 is a C_7 to C_9 alkyl, alkenyl, hydroxyalkyl or hydroxyalkenyl group, preferably a saturated alkyl group, more preferably a saturated, linear, alkyl group; n is a positive integer having a value from 2 to 4, preferably 3; and Y is an alkyl, alkenyl, hydroxy or carboxy substituted alkyl or alkenyl, having from about 2 to about 20 carbon atoms, preferably from about 3 to about 14 carbon atoms. Other preferred synthetic esters conform to the general Formula (X):



wherein R^2 is a C_8 to C_{10} alkyl, alkenyl, hydroxyalkyl or hydroxyalkenyl group; preferably a saturated alkyl group, more preferably a saturated, linear, alkyl group; n and Y are as defined above in Formula (X).

Specific non-limiting examples of suitable synthetic fatty esters for use in the compositions of the present invention include: P-43 (C_8-C_{10} triester of trimethylolpropane), MCP-684 (tetraester of 3,3 diethanol-1,5 pentadiol), MCP 121 (C_8-C_{10} diester of adipic acid), all of which are available from Mobil Chemical Company.

3. Other conditioning agents

Also suitable for use in the compositions herein are the conditioning agents described by the Procter & Gamble Company in U.S. Pat. Nos. 5,674,478, and 5,750,122. Also suitable for use herein are those conditioning agents described in U.S. Pat. Nos. 4,529,586 (Clairol), 4,507,280 (Clairol), 4,663,158 (Clairol), 4,197,865 (L'Oreal), 4,217, 914 (L'Oreal), 4,381,919 (L'Oreal), and 4,422, 853 (L'Oreal).

4. Additional Components

The compositions of the present invention may further include a variety of additional useful components. Preferred additional components include those discussed below:

1. Other Anti-Microbial Actives

The compositions of the present invention may further include one or more anti-fungal or anti-microbial actives in addition to the metal pyrithione salt actives. Suitable anti-microbial actives include coal tar, sulfur, whitfield's ointment, castellani's paint, aluminum chloride, gentian violet, octopirox (piroctone olamine), ciclopirox olamine,

undecylenic acid and it's metal salts, potassium permanganate, selenium sulfide, sodium thiosulfate, propylene glycol, oil of bitter orange, urea preparations, griseofulvin, 8-Hydroxyquinoline ciloquinol, thiobendazole, thiocarbamates, haloprogin, polyenes, hydroxypyridone, morpholine, benzylamine, allylamines (such as terbinafine), tea tree oil, clove leaf oil, coriander, palmarosa, berberine, thyme red, cinnamon oil, cinnamic aldehyde, citronellic acid, hinokitol, ichthyol pale, Sensiva SC-50, Elestab HP-100, azelaic acid, lyticase, iodopropynyl butylcarbamate (IPBC), isothiazalinones such as octyl isothiazalinone and azoles, and combinations thereof. Preferred anti-microbials include itraconazole, ketoconazole, selenium sulphide and coal tar.

a. Azoles

Azole anti-microbials include imidazoles such as benzimidazole, benzothiazole, bifonazole, butaconazole nitrate, climbazole, clotrimazole, croconazole, eberconazole, econazole, elubiol, fenticonazole, fluconazole, flutimazole, isoconazole, ketoconazole, lanoconazole, metronidazole, miconazole, neticonazole, omoconazole, oxiconazole nitrate, sertaconazole, sulconazole nitrate, tioconazole, thiazole, and triazoles such as terconazole and itraconazole, and combinations thereof. When present in the composition, the azole anti-microbial active is included in an amount from about 0.01% to about 5%, preferably from about 0.1% to about 3%, and more preferably from about 0.3% to about 2%, by weight of the composition. Especially preferred herein is ketoconazole.

b. Selenium Sulfide

Selenium sulfide is a particulate anti-dandruff agent suitable for use in the anti-microbial compositions of the present invention, effective concentrations of which range from about 0.1% to about 4%, by weight of the composition, preferably from about 0.3% to about 2.5%, more preferably from about 0.5% to about 1.5%. Selenium sulfide is generally regarded as a compound having one mole of selenium and two moles of sulfur, although it may also be a cyclic structure that conforms to the general formula Se_xS_y, wherein x + y = 8. Average particle diameters for the selenium sulfide are typically less than 15μm, as measured by forward laser light scattering device (e.g. Malvern 3600 instrument), preferably less than 10 μm. Selenium sulfide compounds are described, for example, in U.S. Pat. No. 2,694,668; U.S. Pat. No. 3,152,046; U.S. Pat. No. 4,089,945; and U.S. Pat. No. 4,885,107.

c. Sulfur

Sulfur may also be used as a particulate anti-microbial/anti-dandruff agent in the anti-microbial compositions of the present invention. Effective concentrations of the particulate sulfur are typically from about 1% to about 4%, by weight of the composition, preferably from about 2% to about 4%.

d. Keratolytic Agents

The present invention may further comprise one or more keratolytic agents such as Salicylic Acid.

Additional anti-microbial actives of the present invention may include extracts of melaleuca (tea tree) and charcoal. The present invention may also comprise combinations of anti-microbial actives. Such combinations may include octopirox and zinc pyrithione combinations, pine tar and sulfur combinations, salicylic acid and zinc pyrithione combinations, octopirox and climbasole combinations, and salicylic acid and octopirox combinations, and mixtures thereof.

2. Hair loss prevention and Hair Growth Agents

The present invention may further comprise materials useful for hair loss prevention and hair growth stimulants or agents. Examples of such agents are Anti-Androgens such as Propecia, Dutasteride, RU5884; Anti-Inflammatories such as Glucocortisoids, Macrolides, Macrolides; Anti-Microbials such as Zinc pyrithione, Ketoconazole, Selenium sulfide, Acne Treatments; Immunosuppressives such as FK-506, Cyclosporin; Vasodilators such as minoxidil, Aminexil® and combinations thereof.

3. Sensates

The present invention may further comprise topical sensate materials such as terpenes, vanilloids, alkyl amides, natural extracts and combinations thereof. Terpenes can include menthol and derivatives such as menthyl lactate, ethyl menthane carboxamide, and menthoxypropanediol. Other terpenes can include camphor, eucalyptol, carvone, thymol and combinations thereof. Vanilloids can include capsaicin, zingerone, eugenol, and vanillyl butyl ether. Alkyl amides can include spilanthol, hydroxy alpha-sanschool, pellitorine and combinations thereof. Natural extracts can include peppermint oil, eucalyptol, rosemary oil, ginger oil, clove oil, capsicum, jambu extract, cinnamon oil, laricyl and combinations thereof. Additional topical sensate materials can include methyl salicylate, anethole, benzocaine, lidocane, phenol, benzyl nicotinate, nicotinic acid, cinnamic aldehyde, cinnamyl alcohol, piperine, and combinations thereof.

4. Humectant

The compositions of the present invention may contain a humectant. The humectants herein are selected from the group consisting of polyhydric alcohols, water soluble alkoxylated nonionic polymers, and mixtures thereof. The humectants, when used herein, are preferably used at levels of from about 0.1% to about 20%, more preferably from about 0.5% to about 5%.

Polyhydric alcohols useful herein include glycerin, sorbitol, propylene glycol, butylene glycol, hexylene glycol, ethoxylated glucose, 1, 2-hexane diol, hexanetriol, dipropylene glycol, erythritol, trehalose, diglycerin, xylitol, maltitol, maltose, glucose, fructose, sodium chondroitin sulfate, sodium hyaluronate, sodium adenosine phosphate, sodium lactate, pyrrolidone carbonate, glucosamine, cyclodextrin, and mixtures thereof.

Water soluble alkoxylated nonionic polymers useful herein include polyethylene glycols and polypropylene glycols having a molecular weight of up to about 1000 such as those with CTFA names PEG-200, PEG-400, PEG-600, PEG-1000, and mixtures thereof.

5. Suspending Agent

The compositions of the present invention may further comprise a suspending agent at concentrations effective for suspending water-insoluble material in dispersed form in the compositions or for modifying the viscosity of the composition. Such concentrations range from about 0.1% to about 10%, preferably from about 0.3% to about 5.0%.

Suspending agents useful herein include anionic polymers and nonionic polymers. Useful herein are vinyl polymers such as cross linked acrylic acid polymers with the CTFA name Carbomer, cellulose derivatives and modified cellulose polymers such as methyl cellulose, ethyl cellulose, hydroxyethyl cellulose, hydroxypropyl methyl cellulose, nitro cellulose, sodium cellulose sulfate, sodium carboxymethyl cellulose, crystalline cellulose, cellulose powder, polyvinylpyrrolidone, polyvinyl alcohol, guar gum, hydroxypropyl guar gum, xanthan gum, arabia gum, tragacanth, galactan, carob gum, guar gum, karaya gum, carragheenin, pectin, agar, quince seed (Cydonia oblonga Mill), starch (rice, corn, potato, wheat), algae colloids (algae extract), microbiological polymers such as dextran, succinoglucan, pulleran, starch-based polymers such as carboxymethyl starch, methylhydroxypropyl starch, alginic acid-based polymers such as sodium alginate, alginic acid propylene glycol esters, acrylate polymers such as sodium polyacrylate, polyethylacrylate, polyacrylamide, polyethyleneimine, and inorganic water soluble material such as bentonite, aluminum magnesium silicate, laponite, hectonite,

and anhydrous silicic acid.

Commercially available viscosity modifiers highly useful herein include Carbomers with tradenames Carbopol 934, Carbopol 940, Carbopol 950, Carbopol 980, and Carbopol 981, all available from B. F. Goodrich Company, acrylates/steareth-20 methacrylate copolymer with tradename ACRYSOL 22 available from Rohm and Hass, nonoxynyl hydroxyethylcellulose with tradename AMERCELL POLYMER HM-1500 available from Amerchol, methylcellulose with tradename BENECEL, hydroxyethyl cellulose with tradename NATROSOL, hydroxypropyl cellulose with tradename KLUCEL, cetyl hydroxyethyl cellulose with tradename POLYSURF 67, all supplied by Hercules, ethylene oxide and/or propylene oxide based polymers with tradenames CARBOWAX PEGs, POLYOX WASRs, and UCON FLUIDS, all supplied by Amerchol.

Other optional suspending agents include crystalline suspending agents which can be categorized as acyl derivatives, long chain amine oxides, and mixtures thereof. These suspending agents are described in U.S. Pat. No. 4,741,855. These preferred suspending agents include ethylene glycol esters of fatty acids preferably having from about 16 to about 22 carbon atoms. More preferred are the ethylene glycol stearates, both mono and distearate, but particularly the distearate containing less than about 7% of the mono stearate. Other suitable suspending agents include alkanol amides of fatty acids, preferably having from about 16 to about 22 carbon atoms, more preferably about 16 to 18 carbon atoms, preferred examples of which include stearic monoethanolamide, stearic diethanolamide, stearic monoisopropanolamide and stearic monoethanolamide stearate. Other long chain acyl derivatives include long chain esters of long chain fatty acids (e.g., stearyl stearate, cetyl palmitate, etc.); long chain esters of long chain alkanol amides (e.g., stearamide diethanolamide distearate, stearamide monoethanolamide stearate); and glyceryl esters (e.g., glyceryl distearate, trihydroxystearin, tribehenin) a commercial example of which is Thixin R available from Rheox, Inc. Long chain acyl derivatives, ethylene glycol esters of long chain carboxylic acids, long chain amine oxides, and alkanol amides of long chain carboxylic acids in addition to the preferred materials listed above may be used as suspending agents.

Other long chain acyl derivatives suitable for use as suspending agents include N,N-dihydrocarbyl amido benzoic acid and soluble salts thereof (e.g., Na, K), particularly N,N-di(hydrogenated) C.sub.16, C.sub.18 and tallow amido benzoic acid species of this family, which are commercially available from Stepan Company (Northfield, Ill., USA).

Examples of suitable long chain amine oxides for use as suspending agents

include alkyl dimethyl amine oxides, e.g., stearyl dimethyl amine oxide.
Other suitable suspending agents include primary amines having a fatty alkyl moiety having at least about 16 carbon atoms, examples of which include palmitamine or stearamine, and secondary amines having two fatty alkyl moieties each having at least about 12 carbon atoms, examples of which include dipalmitoylamine or di(hydrogenated tallow)amine. Still other suitable suspending agents include di(hydrogenated tallow)phthalic acid amide, and crosslinked maleic anhydride-methyl vinyl ether copolymer.

6. Other Optional Components

The compositions of the present invention may contain also vitamins and amino acids such as: water soluble vitamins such as vitamin B1, B2, B6, B12, C, pantothenic acid, pantothenyl ethyl ether, panthenol, biotin, and their derivatives, water soluble amino acids such as asparagine, alanin, indole, glutamic acid and their salts, water insoluble vitamins such as vitamin A, D, E, and their derivatives, water insoluble amino acids such as tyrosine, tryptamine, and their salts.

The compositions of the present invention may also contain pigment materials such as inorganic, nitroso, monoazo, disazo, carotenoid, triphenyl methane, triaryl methane, xanthene, quinoline, oxazine, azine, anthraquinone, indigoid, thionindigoid, quinacridone, phthalocianine, botanical, natural colors, including: water soluble components such as those having C. I. Names. The compositions of the present invention may also contain antimicrobial agents which are useful as cosmetic biocides and antidandruff agents including: water soluble components such as piroctone olamine, water insoluble components such as 3,4,4'- trichlorocarbanilide (triclocarban), triclosan and zinc pyrithione.

The compositions of the present invention may also contain chelating agents.

H. Determining Zinc Delivery to Cells

Measurement of the free zinc levels in cells as a function of time is a direct measure of delivery of zinc across the cell wall/membrane. There are many methods available for assessing this process, many are based on use of intracellular fluorescent dyes. An exemplary method is similar to that reported by Turan *et al.* (Turan, B., Fliss, H., Désilets, M. *Am. J. Physiol.* **1997**, *272*, H2095-H2106). In this case, mamallian cells are used, although the procedure is general and can be used with all eukaryotic cells. The general methodology is as follows.

Cells are plated onto a glass cover slip. These immobilized cells are then exposed to a zinc-responsive fluorescent dye such as Fura-2 (Molecular Probes, Inc.) to load the cells with this cell-permeant fluorophore. The cells are then washed to remove dye that is not intracellular. Upon exposure to test treatments, fluorescence is measured as a function of time; in the case of Fura-2, the ratio of fluorescence intensities at 505 nm is taken in response to excitation at 340 and 380 nm. The fluorescence is conveniently measured by using an epifluorescence inverted microscope interfaced to a spectrofluorometer. Fluorescence intensity is proportional to the detected zinc level. In the case of Fura-2, it is useful after maximum fluorscent intensity is achieved to expose the cells to a chelator with a much larger affinity for zinc than calcium (e.g., N,N,N',N'-tetrakis(2-pyridylmethyl)ethylenediamine; TPEN) to assure the measured fluorescent response is due to zinc and not an artifact of calcium transport.

In the present invention, the method as described herein may be used to identify materials with zinc ionophoric behavior. Materials demonstrating this behavior increase zinc transport into cells to a larger extent than would occur with an equal level of a simple zinc salt but in the absence of the zinc ionophore. This would be considered significant (i.e., demonstrating zinc ionophoric behavior) when the increase in fluorescent intensity in the presence of the ionophore vs. exposure to a no zinc ionophoric material control is approximately 1.5-fold, preferably 2-fold higher and most preferably 2.5-fold higher.

I. pH

Preferably, the pH of the compositions of the present invention range from about 2 to about 10, preferably from about 3 to about 9.5, more preferably from about 4 to about 9.

J. Zinc Delivery to Cells Enhances Anti-Fungal Activity

Zinc pyrithione (ZPT) is an effective anti-fungal material and also has zinc ionophoric behavior. Utilizing the procedure for quantitation of intracellular zinc, it has been shown that the combination of zinc salts such as zinc sulfate or zinc oxide with ZPT dramatically increase the rate of zinc transport into model cells (human umbilical vein endothelial cells evaluated with 1 mM ZPT (0.32 ppm) and an equal weight proportion of zinc salt):

	Rate of Zinc Transport (min^{-1})	Antifungal activity of ZPT	
		Amount of ZPT Required (%)*	Amount of zinc salt required (ppm)
ZPT Alone	4	100	0
ZnO Alone	~ 0	-----	500
ZPT + ZnO	22	50	5
$ZnSO_4$ Alone	~0	-----	5000
ZPT + $ZnSO_4$	18	50	5

* 100% ZPT is equivalent to 8ppm (MIC of ZPT alone)

Antifungal activity is assessed microbiologically by a method as described below[1]. The antifungal activity of ZPT is strongly increased by the presence of the additional zinc salts, even though these salts have very weak antifungal activity independently (i.e., high MIC values). This increase in ZPT antifungal activity is seen as a reduced level of ZPT required (50% of amount needed when tested alone) to inhibit cell growth when very low levels (5ppm) of either zinc salt is present.

Without being bound by theory, it is believed that the increased zinc transport when ZPT is combined with zinc salts is responsible for the increased antifungal activity of the combination vs. ZPT alone. This establishes the relationship between zinc transport and antifungal activity, thereby supporting the finding that zinc ionophoric materials are effective antifungal materials.

1. The Minimum Inhibitory Concentration is indicative of anti-fungal efficacy. Generally, the lower the value of the composition, the better its anti-fungal efficacy, due to increased inherent ability of the anti-dandruff agent to inhibit the growth of microorganisms.

Malassezia furfur was grown in a flask containing mDixon medium (see E. Gueho, et al. Antoinie Leeuwenhoek (1996), no. 69, 337-55, which description is incorporated by reference herein). Dilutions of solubilized anti-microbial active were then added to test tubes containing molten mDixon agar. *M. furfur* inoculum was added to each tube of molten agar, the tube vortexed, and the contents poured into separate sterile petri dishes. After the plates are incubated, they were observed for visible *M.*

furfur growth. The lowest tested dilution of anti-microbial active that yields no growth is defined as the Minimal Inhibitory Concentration (MIC).

Equipment/Reagents

Microbe	*Malassezia furfur* (ATCC 14521)
Erlenmeyer flask	250ml
Agar medium	9.5ml mDixon agar per concentration per active tested
Solvent	water, dimethyl sulfonyl oxide ("DMSO")
Zinc pyridinethione	ZPT having an average particle size of about 2.5μm,
Test tubes	2 tubes per anti-microbial active per concentration per active tested, sterilized, size = 18mm x 150mm
Petri dishes	2 dishes per anti-microbial active per concentration per active tested, sterilized, size = 15mm x 100mm

Experimental procedure

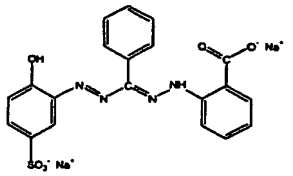
1) *Malassezia furfur* was grown in a 250 ml Erlenmeyer flask containing 100 ml "mDIXON" medium at 320 rpm and 30°C until turbid.
2) Selected dilutions were prepared using an appropriate dilution series, of the anti-microbial active or combination in solvent, which allowed the sample active to be solubilized prior to addition to the final test agar. For each concentration of the ZPT samples, the solvent was "DMSO"; for other samples, the solvent was water or "DMSO" or other suitable solvent.
3) 0.25 ml dilutions of anti-microbial active were added to test tubes containing 9.5 ml molten "mDIXON" agar (held at 45°C in a water bath).
4) 0.25 *M. furfur* inoculum (adjusted to 5 x 10^5 cfu/ml by direct count) was added to each test tube of molten agar.
5) Each tube was vortexed, and the contents poured into separate petri dishes.
6) After the agar solidified, the plates inverted and incubated at 30° for 5 days.
7) The plates were then observed for visible *M. furfur* growth.

K. Classification of Zinc-Containing Materials According to their Zinc Availability

Zinc-containing materials (ZCMs) differ with respect to how strongly the zinc ion (Zn^{2+}) is held by counterions in the crystal lattice. The benefits discussed herein depend upon having available Zn^{2+}. To determine which ZCMs provide sufficient labile Zn^{2+} and those that do not, a test was developed using a metallochromic dye which changes color

upon coordinating Zn^{2+}. The response is a binary visual assessment of whether or not the color changes indicating zinc-binding. If the color changes, the ZCM is classified as having available Zn^{2+} whereas if it does not change, the ZCM is not useful for this invention.

The method is based on the commercial metallochromic dye zincon. Zincon changes from an orange color to blue upon binding zinc and provides the basis for detecting available Zn^{2+}:



Na-Zincon + Zn^{2+} → Zn-Zincon

Orange-ish Blue (λ_{max} 620)

The specific procedure involves making a stock solution of zincon in ethanol (~50mg/10 ml ethanol). The ZCM is then added to water (~30 mg/10 ml water) and agitated (pH range should be 7-11). Three to four drops of zincon solution are then added to the ZCM in water, agitated and a visual assessment of color change made.

Using this methodology, the following ZCMs are examples of those that have available zinc: zinc chloride, zinc sulfate, zinc citrate, zinc oxide, zinc acetate, zinc stearate, zinc lactate, zinc salicylate, zinc arginine, zinc histadine, zinc hexaborate, zinc hydroxide, zinc oxalate, zinc monoglycerolate and the like. Examples of ZCMs not having available Zn^{2+} are zinc EDTA, zinc sulfide, zinc phytate and other materials with very tightly bound zinc.

In an embodiment of the present invention, the composition comprises from 5% to 50% of a surfactant; a zinc containing material wherein zinc availability is measured by a zinc ion reacting with a metallochromic dye zincon to give a dye color change from orange to blue. In another embodiment of the present invention, the composition comprises from 5% to 50% of a surfactant; a zinc containing material wherein zinc availability is measured by a zinc ion reacting with a metallochromic dye zincon to give a dye color change from orange to blue and a zinc ionophoric material.

L. Methods of Manufacture

The compositions of the present invention may be prepared by any known or otherwise effective technique, suitable for providing an anti-microbial composition provided that the resulting composition provides the excellent anti-microbial benefits described herein. Methods for preparing the anti-dandruff and conditioning shampoo embodiments of the present invention include conventional formulation and mixing techniques. A method such as that described in U.S. Pat. No. 5,837,661, could be employed, wherein the anti-microbial agent of the present invention would typically be added in the same step as the silicone premix is added in the U.S. Pat. No. 5,837,661 description.

M. Methods of Use

The compositions of the present invention may be used in direct application to the skin or in a conventional manner for cleansing skin and hair and controlling microbial infection (including fungal, viral, or bacterial infections) on the skin or scalp. The present invention may be used for treating or cleansing of the skin or hair of animals as well. Directly applied compositions, such as powders, are used by applying an effective amount of the composition, typically form 1 to 20g, to the skin; for example, to the feet. The cleansing compositions herein are useful for cleansing the hair and scalp, and other areas of the body such as underarm, feet, and groin areas and for any other area of skin in need of treatment. An effective amount of the composition, typically from about 1g to about 50g, preferably from about 1g to about 20g of the composition, for cleansing hair, skin or other area of the body, is topically applied to the hair, skin or other area that has preferably been wetted, generally with water, and then rinsed off. Application to the hair typically includes working the shampoo composition through the hair.

A preferred method for providing anti-microbial (especially anti-dandruff) efficacy with a shampoo embodiment comprises the steps of: (a) wetting the hair with water, (b) applying an effective amount of the anti-microbial shampoo composition to the hair, and (c) rinsing the anti-microbial shampoo composition from the hair using water. These steps may be repeated as many times as desired to achieve the cleansing, conditioning, and anti-microbial/anti-dandruff benefits sought.

It is also contemplated that when the anti-microbial active employed is zinc pyrithione, and/or if other optional hair growth regulating agents are employed, the anti-microbial compositions of the present invention, may, provide for the regulation of

growth of the hair. The method of regularly using such shampoo compositions comprises repeating steps a, b, and c (above).

A further embodiment of the present invention comprises a method comprising the steps of (a) wetting the hair with water, (b) applying an effective amount of a shampoo composition comprising a zinc ionophore, (c) rinsing the shampoo compositions from the hair using water; (d) applying an effective amount of a conditioner composition comprising a zinc containing material according to the present invention; (e) rinsing the conditioner composition from the hair using water. In a further embodiment, this method could be conducted wherein steps d and b are reversed. In a further embodiment, steps b and d can vary and be a shampoo, hair lotions, hair sprays, hair tonics, conditioning treatments, gels, mousses and dressings, and the like. A preferred embodiment of the above mentioned method includes a shampoo composition comprising zinc pyrithione and a conditioner composition comprising zinc oxide.

A further embodiment of the present invention comprises a method of treating athlete's foot (tinea pedis) comprising treating the effected area with a composition comprising comprising a zinc ionophoric material; a method of treating microbial infections comprising treating the effected area with a composition comprising a zinc ionophoric material; a method of improving the appearance of a scalp comprising treating the effected area with a composition comprising a zinc ionophoric material; a method of treating fungal infections comprising treating the effected area with a composition comprising a zinc ionophoric material; a method of treating dandruff comprising treating the effected area with a composition comprising a zinc ionophoric material; a method of treating diaper dermatitis and candidiasis comprising treating the effected area with a composition comprising a zinc ionophoric material; a method of treating tinea capitis comprising treating the effected area with a composition comprising a zinc ionophoric material; a method of treating yeast infections comprising treating the effected area with a composition comprising a zinc ionophoric material; a method of treating onychomycosis (nail infections) comprising treating the effected area with a composition comprising a zinc ionophoric material; a method for providing anti-dandruff efficacy comprising applying to the hair and scalp materials having zinc ionophoric behavior.

A further embodiment of the present invention comprises compositions wherein a zinc ionophoric material may be present alone or in combination with a zinc containing material.

N. Examples

The following examples further describe and demonstrate the preferred embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration, and are not to be construed as limitations of the present invention since many variations thereof are possible without departing from its scope.

The composition of the invention can be made by mixing one or more selected metal ion sources and one or more metal salts of pyrithione in an appropriate media or carrier, or by adding the individual components separately to the skin or hair cleansing compositions. Useful carriers are discussed more fully above.

1. Topical Compositions

All exemplified compositions can be prepared by conventional formulation and mixing techniques. Component amounts are listed as weight percents and exclude minor materials such as diluents, filler, and so forth. The listed formulations, therefore, comprise the listed components and any minor materials associated with such components. As used herein, "minors" refers to those optional components such as preservatives, viscosity modifiers, pH modifiers, fragrances, foam boosters, and the like. As is apparent to one of ordinary skill in the art, the selection of these minors will vary depending on the physical and chemical characteristics of the particular ingredients selected to make the present invention as described herein. Other modifications can be undertaken by the skilled artisan without departing from the spirit and scope of this invention. These exemplified embodiments of the anti-microbial shampoo, anti-microbial conditioner, anti-microbial leave-on tonic, and anti-microbial foot powder compositions of the present invention provide excellent anti-microbial efficacy.

Antimicrobial Shampoo - Examples 1-40

A suitable method for preparing the anti-microbial shampoo compositions described in Examples 1-40 (below) follows:

About one-third to all of the sodium laureth sulfate (added as 25wt% solution) and acid are added to a jacketed mix tank and heated to about 60°C to about 80°C with slow agitation to form a surfactant solution. The pH of this solution is about 7.5. Sodium benzoate, Cocoamide MEA and fatty alcohols, (where applicable), are added to the tank and allowed to disperse. Ethylene glycol distearate ("EGDS") is added to the mixing vessel and allowed to melt (where applicable). After the EGDS is melted and dispersed, Kathon CG is added to the surfactant solution. The resulting mixture is cooled to about 25°C to about 40°C and collected in a finishing tank. As a result of this cooling step, the

EGDS crystallizes to form a crystalline network in the product (where applicable). The remainder of the sodium laureth sulfate and other components, including the silicone and anti-microbial agent(s), are added to the finishing tank with agitation to ensure a homogeneous mixture. Polymers (cationic or nonionic) are dispersed in water or oils as an about 0.1% to about 10% dispersion and/or solution and then added to the final mix. ZnO or Zinc Hydroxy carbonate ("ZHC") can be added to a premix of surfactants or water with or without the aid of a dispersing agent via conventional powder incorporation and mixing techniques into the final mix. Adjustment of ZnO particle size can be affected by various conventional mixing techniques obvious to one skilled in the art. Once all components have been added, additional viscosity modifiers may be added, as needed, to the mixture to adjust product viscosity to the extent desired.

	Weight Percent									
Components	Example 1	Example 2	Example 3	Example 4	Example 5	Example 6	Example 7	Example 8	Example 9	Example 10
Ammounium Laureth Sulfate	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00
Ammounium Lauryl Sulfate	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
Sodium Laureth Sulfate										
Sodium Lauryl Sulfate										
Cocamidopropyl Betaine										
EGDS	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
CMEA	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800
Cetyl Alcohol	0.900	0.900	0.900	0.900	0.900	0.900	0.900	0.900	0.900	0.900
Guar Hydroxy Propyltrimonium Chloride (1)	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500
Guar Hydroxy Propyltrimonium Chloride (2)										
Guar Hydroxy Propyltrimonium Chloride (3)										
Polyquaterium-10 (4)										
Polyquaterium-10 (5)										
PEG-7M (6)										
Dimethicone (7)	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35	1.35
Dimethicone (8)										
Trimethylolpropane tricaprylate/tricaprate (9)										
Hydrogenated Polydecene (10)										
ZPT (11)	2.00	1.00					1.00	1.00		
8-hydroxyquinoline			1.00	2.00				1.00	1.00	
Zinc 8-hydroxyquinoline (12)					1.00	2.00				1.00
Zinc Oxide										
Zinc Carbonate Basic										
Zinc Sulfate							3.00	3.00	3.00	3.00
Sodium Bicarbonate										
Hydrochloric Acid										
Sodium Citrate	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400

Citric Acid	0.0400	0.0400	0.0400	0.0400	0.0400	0.0400	0.0400	0.0400	0.0400	0.0400
Magnesium Sulfate										
Sodium Chloride	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800
Perfume	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750
Sodium Benzoate	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Kathon	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008
Benzyl Alcohol	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

	Weight Percent									
Components	Example 11	Example 12	Example 13	Example 14	Example 15	Example 16	Example 17	Example 18	Example 19	Example 20
Ammounium Laureth Sulfate										
Ammounium Lauryl Sulfate										
Sodium Laureth Sulfate	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00
Sodium Lauryl Sulfate	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00
Cocamidopropyl Betaine										
EGDS	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
CMEA	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	1.600
Cetyl Alcohol	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600
Guar Hydroxy Propyltrimonium Chloride (1)	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500
Guar Hydroxy Propyltrimonium Chloride (2)										
Guar Hydroxy Propyltrimonium Chloride (3)										
Polyquaterium-10 (4)										
Polyquaterium-10 (5)										
PEG-7M (6)										
Dimethicone (7)	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85
Dimethicone (8)										
Trimethylolpropane tricaprylate/tricaprate (9)										
Hydrogenated Polydecene (10)										
ZPT (11)	1.00	1.00		1.00	1.00			1.00	1.00	1.00
8-hydroxyquinoline		1.00	1.00			1.00				
Zinc 8-hydroxyquinoline (12)							1.00			
Zinc Oxide	1.20	1.20	1.20	1.20	1.20	1.20	1.20	1.20	1.20	1.20
Zinc Carbonate Basic										
Zinc Sulfate										
Sodium Bicarbonate	0.20	0.20	0.20	0.10	0.05	0.05	0.05	0.25		0.20
Hydrochloric Acid	0.78	0.78	0.78	0.53	0.40	0.40	0.40	0.91	0.28	0.78
Sodium Citrate										
Citric Acid										
Magnesium Sulfate	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28

Sodium Chloride	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800
Perfume	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750
Sodium Benzoate	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Kathon	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008
Benzyl Alcohol	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

	Weight Percent									
Components	**Example 21**	**Example 22**	**Example 23**	**Example 24**	**Example 25**	**Example 26**	**Example 27**	**Example 28**	**Example 29**	**Example 30**
Ammounium Laureth Sulfate										
Ammounium Lauryl Sulfate										
Sodium Laureth Sulfate	10.00	10.00	10.00	12.50	10.00	10.00	10.00	10.00	10.00	10.00
Sodium Lauryl Sulfate	6.00	6.00	6.00	1.50	6.00	6.00	6.00	6.00	6.00	6.00
Cocamidopropyl Betaine				2.70				2.00		
EGDS	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
CMEA	1.600	1.600	1.600	0.800	0.800	0.800	1.600	0.800	0.800	0.800
Cetyl Alcohol	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600
Guar Hydroxy Propyltrimonium Chloride (1)	0.500			0.500	0.500	0.500	0.500	0.500	0.500	0.500
Guar Hydroxy Propyltrimonium Chloride (2)		0.500								
Guar Hydroxy Propyltrimonium Chloride (3)			0.500							
Polyquaterium-10 (4)										
Polyquaterium-10 (5)										
PEG-7M (6)	0.200					0.200	0.200			
Dimethicone (7)	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85
Dimethicone (8)										
Trimethylolpropane tricaprylate/tricaprate (9)										
Hydrogenated Polydecene (10)										
ZPT (11)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
8-hydroxyquinoline										
Zinc 8-hydroxyquinoline (12)										
Zinc Oxide	1.20	1.20	1.20	1.20						
Zinc Carbonate Basic					1.61	1.61	1.61	1.61	0.80	0.40
Zinc Sulfate										
Sodium Bicarbonate	0.20	0.20	0.20	0.20						
Hydrochloric Acid	0.78	0.78	0.78	0.78	0.42	0.42	0.42	0.42	0.42	0.42
Sodium Citrate										
Citric Acid										
Magnesium Sulfate	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28
Sodium Chloride	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800
Perfume	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750
Sodium Benzoate	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250

Kathon	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008
Benzyl Alcohol	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

	Weight Percent									
Components	Example 31	Example 32	Example 33	Example 34	Example 35	Example 36	Example 37	Example 38	Example 39	Example 40
Ammounium Laureth Sulfate										
Ammounium Lauryl Sulfate										
Sodium Laureth Sulfate	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	12.50
Sodium Lauryl Sulfate	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	6.00	1.50
Cocamidopropyl Betaine										2.70
EGDS	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50	1.50
CMEA	0.800	0.800	0.800	0.800	0.800	1.600	0.800	0.800	1.600	0.800
Cetyl Alcohol	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600	0.600
GuarHydroxy Propyltrimonium Chloride (1)	0.500	0.500	0.500	0.500	0.500	0.500				0.500
GuarHydroxy Propyltrimonium Chloride (2)								0.500		
GuarHydroxy Propyltrimonium Chloride (3)							0.500		0.500	
Polyquaterium-10 (4)										
Polyquaterium-10 (5)										
PEG-7M (6)										
Dimethicone (7)	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85	0.85
Dimethicone (8)										
Trimethylolpropane tricaprylate/tricaprate (9)										
Hydrogenated Polydecene (10)										
ZPT (11)		0.50			2.00	1.00	1.00	1.00	1.00	1.00
8-hydroxyquinoline	1.00									
Zinc 8-hydroxyquinoline (12)			1.00	2.00						
Zinc Oxide										
Zinc Carbonate Basic	1.61	0.80	1.61	1.61	1.61	1.61	1.61	1.61	1.61	1.61
Zinc Sulfate										
Sodium Bicarbonate										
Hydrochloric Acid	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42	0.42
Sodium Citrate										
Citric Acid										
Magnesium Sulfate	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28
Sodium Chloride	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800	0.800
Perfume	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750
Sodium Benzoate	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Kathon	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008	0.0008
Benzyl Alcohol	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225	0.0225

Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

(1) Guar having a molecular weight of about 400,000, and having a charge density of about 0.84 meq/g, available from Aqualon.
(2) Guar having a molecular weight of about 400,000, and having a charge density of about 2.0 meq/g, available from Aqualon.
(3) Cationic guar Jaguar C17 available from Rhodia
(4) Polymer JR30M available from Amerchol
(5) Polymer LR400 available from Amerchol
(6) Polyox WSR N-750 available from Amerchol
(7) Viscasil 330M available from General Electric Silicones
(8) DC1664 available from Dow Corning Silicones
(9) Modil P43 available from Mobil.
(10) Puresyn 6 available from Mobil.
(11) ZPT having an average particle size of about 2.5 m, available from Arch/Olin.
(12) Zinc oxinate available from Pfaltz & Bauer

Hair Conditioning Composition - Examples 42-83

A suitable method for preparing the anti-microbial hair conditioning compositions described in Examples 42-83 (below) by conventional formulation and mixing techniques follows:

When included in the composition, polymeric materials such as polypropylene glycol are dispersed in water at room temperature to make a polymer solution, and heated up to above 70°C. Amidoamine and acid, and when present, other cationic surfactants, ester oil of low melting point oil are added in the solution with agitation. Then high melting point fatty compound, and when present, other low melting point oils and benzyl alcohol are also added in the solution with agitation. The mixture thus obtained is cooled down to below 60°C, and the remaining components such as zinc pyrithione, zinc containing material, zinc ionophoric material and silicone compound are added with agitation, and further cooled down to about 30°C.

A triblender and/or mill can be used in each step, if necessary to disperse the materials. Alternatively, up to 50% of the acid can be added after cooling below 60°C.

The embodiments disclosed herein have many advantages. For example, they can provide effective anti-microbial, especially anti-dandruff, efficacy, while not deteriorating conditioning benefits such as wet hair feel, spreadability, and rinsability, as well as providing glossiness, and dry combing.

Components	Example 42	Example 43	Example 44	Example 45	Example 46	Example 47	Example 48	Example 49	Example 50	Example 51	Example 52
L-Glutamic Acid	0.412	0.412	0.412	0.640	0.640	0.640	0.412	0.412	0.412	0.412	0.412
Stearamidopropyldimethylamine	1.600	1.600	1.600	2.000	2.000	2.000	1.600	1.600	1.600	1.600	1.600
Behentrimonium Chloride											
Quaterium-18											
Cetyl Alcohol	2.000	2.000	2.000	2.500	2.500	2.500	2.000	2.000	2.000	2.000	2.000
Stearyl Alcohol	3.600	3.600	3.600	4.500	4.500	4.500	3.600	3.600	3.600	3.600	3.600
Cetearyl Alcohol											
Polysorbate 60											
Glyceral Monostearate											

Oleyl Alcohol											
Hydroxyethylcellulose											
Peg 2M (1)											
Dimethicone (2)										0.200	0.200
Dimethicone (3)	0.500	0.500	0.500	0.630	0.630	0.630	0.500	0.500	0.500		
Cyclopentasiloxane (3)	2.860	2.860	2.860	3.570	3.570	3.570	2.860	2.860	2.860		
Benzyl Alcohol	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400
Methyl Paraben	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200
Propyl Paraben	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Phenoxy Ethanol	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300
Sodium Chloride	0.010	0.010	0.010	0.010	0.010	0.010	0.010	0.010	0.010	0.010	0.010
Zinc Pyrithione (4)	2.000			1.000			0.500			2.000	2.000
8-Hydroxyquinoline		2.000			1.000			0.500			
Zinc 8-Hydroxyquinoline (5)			2.000			1.000			0.500		
Zinc Oxide											1.200
Zinc Carbonate Basic											
Zinc Sulfate											
Citric Acid	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130
Kathon											
Perfume	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400
Sodium Hydroxide											
Isopropyl Alcohol											
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

(1) **Polyox WAR N-10 available from Amerchol Corp.**
(2) **10,000cps Dimethicone TSF451-1MA available from GE**
(3) **15/85 Dimethicone/ Cyclomethicone Blend available from GE**
(4) ZPT having an average particle size of about 2.5 m, available from Arch/Olin.
(5) Zinc oxinate available from Pfaltz & Bauer

Components	Example 53	Example 54	Example 55	Example 56	Example 57	Example 58	Example 59	Example 60	Example 61	Example 62	Example 63
L-Glutamic Acid	0.412	0.412	0.412	0.412	0.412	0.412	0.412	0.412	0.412	0.412	0.412
Stearamidopropyldimethylamine	1.600	1.600	1.600	1.600	1.600	1.600	1.600	1.600	1.600	1.600	1.600
Behentrimonium Chloride											
Quaterium-18											
Cetyl Alcohol	2.000	2.000	2.000	2.000	2.000	2.000	2.000	2.000	2.000	2.000	2.000
Stearyl Alcohol	3.600	3.600	3.600	3.600	3.600	3.600	3.600	3.600	3.600	3.600	3.600
Cetearyl Alcohol											
Polysorbate 60											
Glyceral Monostearate											
Oleyl Alcohol											
Hydroxyethylcellulose											
Peg 2M (1)											
Dimethicone (2)	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200
Dimethicone (3)											
Cyclopentasiloxane (3)											
Benzyl Alcohol	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400
Methyl Paraben	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200

Propyl Paraben	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Phenoxy Ethanol	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300
Sodium Chloride	0.010	0.010	0.010	0.010	0.010	0.010	0.010	0.010	0.010	0.010	0.010
Zinc Pyrithione (4)			2.000			2.000					
8-Hydroxyquinoline	2.000			2.000			2.000		1.000	0.500	
Zinc 8-Hydroxyquinoline (5)		2.000			2.000			2.000			1.000
Zinc Oxide	1.200	1.200									
Zinc Carbonate Basic			1.610	1.610	1.610						
Zinc Sulfate						3.000	3.000	3.000	3.000	3.000	3.000
Citric Acid	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130
Kathon											
Perfume	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400
Sodium Hydroxide											
Isopropyl Alcohol											
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

(1) Polyox WAR N-10 available from Amerchol Corp.
(2) 10,000cps Dimethicone TSF451-1MA available from GE
(3) 15/85 Dimethicone/ Cyclomethicone Blend available from GE
(4) ZPT having an average particle size of about 2.5 m, available from Arch/Olin.
(5) Zinc oxinate available from Pfaltz & Bauer

Components	Example 64	Example 65	Example 66	Example 67	Example 68	Example 69	Example 70	Example 71	Example 72	Example 73	Example 74
L-Glutamic Acid	0.412										
Stearamidopropyldimethy lamine	1.600	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
Behentrimonium Chloride											
Quaterium-18		0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750	0.750
Cetyl Alcohol	2.000	0.960	0.960	0.960	0.960	0.960	0.960	0.960	0.960	0.960	0.960
Stearyl Alcohol	3.600	0.640	0.640	0.640	0.640	0.640	0.640	0.640	0.640	0.640	0.640
Cetearyl Alcohol		0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500
Polysorbate 60		0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500
Glyceral Monostearate		0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Oleyl Alcohol		0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Hydroxyethylcellulose		0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250	0.250
Peg 2M (1)		0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500	0.500
Dimethicone (2)	0.200								0.252	0.252	0.252
Dimethicone (3)		0.630	0.630	0.630	0.630	0.630	0.630	0.630			
Cyclopentasiloxane (3)		3.570	3.570	3.570	3.570	3.570	3.570	3.570			
Benzyl Alcohol	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400
Methyl Paraben	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200
Propyl Paraben	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Phenoxy Ethanol	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300
Sodium Chloride	0.010										
Zinc Pyrithione (4)		2.000			1.000				2.000		
8-Hydroxyquinoline			2.000			1.000				2.000	
Zinc 8-Hydroxyquinoline (5)	0.500			2.000			1.000				2.000
Zinc Oxide											

Zinc Carbonate Basic											
Zinc Sulfate	3.000										
Citric Acid	0.130	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200
Kathon											
Perfume	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400
Sodium Hydroxide											
Isopropyl Alcohol											
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

(1) Polyox WAR N-10 available from Amerchol Corp.
(2) 10,000cps Dimethicone TSF451-1MA available from GE
(3) 15/85 Dimethicone/ Cyclomethicone Blend available from GE
(4) ZPT having an average particle size of about 2.5 m, available from Arch/Olin.
(5) Zinc oxinate available from Pfaltz & Bauer

Components	Example 75	Example 76	Example 77	Example 78	Example 79	Example 80	Example 81	Example 82	Example 83
L-Glutamic Acid									
Stearamidopropyldimethylamine	1.000	1.000	1.000						
Behentrimonium Chloride				3.380	3.380	3.380	3.380	3.380	3.380
Quaterium-18	0.750	0.750	0.750						
Cetyl Alcohol	0.960	0.960	0.960	2.320	2.320	2.320	2.320	2.320	2.320
Stearyl Alcohol	0.640	0.640	0.640	4.180	4.180	4.180	4.180	4.180	4.180
Cetearyl Alcohol	0.500	0.500	0.500						
Polysorbate 60	0.500	0.500	0.500						
Glyceral Monostearate	0.250	0.250	0.250						
Oleyl Alcohol	0.250	0.250	0.250						
Hydroxyethylcellulose	0.250	0.250	0.250						
Peg 2M (1)	0.500	0.500	0.500						
Dimethicone (2)	0.252	0.252	0.252						
Dimethicone (3)				0.630	0.630	0.630	0.630	0.630	0.630
Cyclopentasiloxane (3)				3.570	3.570	3.570	3.570	3.570	3.570
Benzyl Alcohol	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400	0.400
Methyl Paraben	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200	0.200
Propyl Paraben	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100	0.100
Phenoxy Ethanol	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300	0.300
Sodium Chloride									
Zinc Pyrithione (4)	2.000			2.000			2.000		
8-Hydroxyquinoline		2.000			2.000			2.000	
Zinc 8-Hydroxyquinoline (5)			2.000			2.000			2.000
Zinc Oxide							1.200		
Zinc Carbonate Basic	1.610	1.610	1.610					1.610	
Zinc Sulfate									3.000
Citric Acid	0.200	0.200	0.200						
Kathon									
Perfume	0.400	0.400	0.400	0.300	0.300	0.300	0.300	0.300	0.300
Sodium Hydroxide				0.014	0.014	0.014	0.014	0.014	0.014
Isopropyl Alcohol				0.507	0.507	0.507	0.507	0.507	0.507
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

(1) Polyox WAR N-10 available from Amerchol Corp.
(2) 10,000cps Dimethicone TSF451-1MA available from GE
(3) 15/85 Dimethicone/ Cyclomethicone Blend available from GE
(4) ZPT having an average particle size of about 2.5 m, available from Arch/Olin.
(5) Zinc oxinate available from Pfaltz & Bauer

Anti-Microbial Leave-In Hair Tonic - Examples 84-90

A suitable method for preparing the anti-microbial leave-in hair tonic compositions described in Examples 84-90 (below) follows:

Add most of the formula water; with stirring, add carbomer and mix until fully dispersed. In a separate vessel, add ethanol and then molten PEG-60 hydrogenated castor oil and perfume. Transfer this to main mix tank with agitation. Add other water soluble ingredients, minors, zinc pyrithione, zinc containing materials and/or zinc ionophoric materials. Slowly add styryl silicone and let stir. Add triethanolamine slowly with stirring.

	Weight Percent						
Components	**Example 84**	**Example 85**	**Example 86**	**Example 87**	**Example 88**	**Example 89**	**Example 90**
Carbomer	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Triethanolamine	0.30	0.30	0.30	0.30	0.30	0.30	0.30
Ethanol	25.00	25.00	25.00	25.00	25.00	25.00	25.00
Zinc Pyrithione (1)	0.10						
Zinc 8-hydroxyquinoline (2)		0.10		0.10		0.10	
8-hydroxyquinoline			0.10		0.10		0.10
Camphor	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Menthol	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Panthenol	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Pantyl Ethyl Ether	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Zinc Sulfate				0.20	0.20		
Zinc Oxide						0.20	
Zinc Carbonate Basic							0.20
Lactic Acid	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Styryl Silicone	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Ceteareth-20	0.15	0.15	0.15	0.15	0.15	0.15	0.15
PEG-60 Hydrogenated Castor Oil	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Perfume	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

(1) ZPT having an average particle size of about 2.5 m, available from Arch/Olin.
(2) Zinc oxinate available from Pfaltz & Bauer

Anti-microbial Foot Powder - Example 91-94

The foot powder composition of Examples 91-94 is prepared by thoroughly mixing the ingredients in a mixing vessel. The powder may then be ground and/or sifted if necessary.

	Weight Percent			
Components	Example 91	Example 92	Example 93	Example 94
Talc	73.25%	73.25%	73.25%	73.7%
Calcium Propionate	15.0	15.0	15.0	15.0
Zinc Propionate	5.0	5.0	5.0	5.0
Zinc Caprylate	5.0	5.0	5.0	5.0
Propionic Acid	0.25	0.25	0.25	0.25
Zinc Sulfate	0.50	0.50	0.50	
Zinc Pyrithione (1)	1.0			
Zinc 8-hydroxyquinoline (2)		1.0		
8-hydroxyquinoline			1.0	1.0
	100.00	100.00	100.00	100.00

(1) ZPT having an average particle size of about 2.5 m, available from Arch/Olin.
(2) Zinc oxinate available from Pfaltz & Bauer

Oil-in Water cream/lotion - Examples 94-98

	Weight Percent				
Components	Example 94	Example 95	Example 96	Example 97	Example 98
Oil Phase					
Mineral oil	15.0	20.0	20.0	20.0	20.0
Polysorbate	2.0	3.0	3.0	3.0	3.0
Aqueous Phase					
Zinc Oxide	0.2	0.2	0.2		
Zinc pyrithione (1)	1.0				
Zinc 8-hydroxyquinoline (2)		1.0		1.0	
8-hydroxyquinoline			1.0		1.0
Preservative	0.3	0.3	0.3	0.3	0.3
Perfume	0.2	0.2	0.2	0.2	0.2
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

(1) ZPT having an average particle size of about 2.5 m, available from Arch/Olin.
(2) Zinc oxinate available from Pfaltz & Bauer

Evaluation of Several Zinc Ionophoric Materials - Example 99

Anti-fungal activity of materials having zinc ionophoric behavior was screened by measurement of minimum inhibitory concentrations (MIC's) against Malassezia furfur. The lower the MIC, the more potent the anti-fungal activity.

Material	MIC (ppm)
Enterovioform	25
5,7-D-Br-8-HQ	25
Sterosan	100
Diodoquin	25
Lasalocid	> 1000
A23187	> 13
TBTDS	> 1000

For perspective, ZPT has an MIC of 8 ppm and several of these materials have potency that begins to approach this potency and would, therefore, be expected to provide an anti-dandruff benefit (either alone or in combination with other actives such as ZPT). There is most likely sufficient zinc in the growth medium to meet the needs of the ionophore, but additional sources of zinc may be added.

O. Other Preferred Embodiments

Other preferred embodiments of the present invention include the following:

An embodiment of the present invention relates to a method for delivering excess zinc to eukaryotic cells to inhibit the metabolism of the cell, the method comprising treating the cells with a ZIM that is capable of delivering a zinc ion across a cellular membrane wherein the minimum inhibitory concention (MIC) of the zinc ionophoric material is less than about 500 parts per million (ppm). Preferably, the ZIM is in combination with a zinc containing material such that there is an increase in the intracellular zinc level by 1.5 folds more than would occur in the absence of the ZIM. In a further embodiment, the ZIM has a potency against target microorganisms such that the minimum inhibitory concentration is below about 5000 parts per million. In a further embodiment, the ZIM is present as a zinc salt of the zinc ionophoric material. Preferably, the ZIM is a zinc ionophore, hydrophobic zinc material, or mixtures thereof.

More preferably, the ZIM is a polyvalent metal salt of a pyrithione, dithiocarbamate, heterocyclic amine, nonsteriodal anti-inflammatory compound, naturally occurring zinc ionophoric material, or derivative thereof, bio-molecule, or pepetide, sulfur-based compound, transport enhancer or mixtures thereof.

In a preferred embodiment, the dithiocarbamate is a pyrrolidine dithiocarbamate, diethyldithiocarbamate, zinc diethyldithiocarbamate, disulfiram, dimethyldithiocarbamate, zinc dimethyldithiocarbamate, or mixtures thereof.

In a preferred embodiment, the heterocyclic amine is 8-hydroxyquinoline, 5,7-Diiodo-8-hydroxyquinoline, and 5,7-Dichloro-8-hydroxyquinoline, 5-chloro-7-iodo-8-hydroxyquinoline, chloroquinaldol, 2-methyl-5,7-Dichoro-8-hydroxyquinoline, 5-7-dibromo-8-hydroxyquinoline, or mixtures thereof.

In a preferred embodiment, the ZIM is pyrithione or a zinc salt of pyrithione; more preferably zinc pyrithione.

In a preferred embodiment, bio-molecules and peptides are lasalocid (X537A), A23187 (calcimycin), 4-BR A23187, ionomycin, cyclosporin A, or mixtures thereof.

In a preferred embodiment, the sulfur-based compound is tetra-n-butyl thiuram disulfide.

In a preferred embodiment, the transport enhancer is albumin, histidine, arachidonic acid, picolinic acid, dihydroxyvitamin D_3, ethylmaltol, or mixtures thereof.

In a preferred embodiment, the ZIM is present in combination with a source of zinc ions. Preferably, the source of zinc ions is an inorganic material, natural zinc containing material, ore, mineral, organic salt, polymeric salt, physically adsorbed form material, or mixtures thereof

In a preferred embodiment, the inorganic material is zinc aluminate, zinc carbonate, zinc oxide and materials containing zinc oxide, zinc phosphates , zinc selenide, zinc sulfide, zinc silicates, zinc silicofluoride, zinc borate, zinc hydroxide, zinc hydroxy sulfate, or mixtures thereof.

In a preferred embodiment, the zinc containing material is sphalerite, wurtzite, smithsonite, franklinite, zincite, willemite, troostite, or mixtures thereof.

In a preferred embodiment, the organic salt is a zinc fatty acid salt, zinc salt of alkyl sulfonic acid, zinc naphthenate, zinc tartrate, zinc tannate, zinc phytate, zinc monoglycerolate, zinc allantoinate, zinc urate, zinc amino acid salt, or mixtures thereof.

In a preferred embodiment, the physically adsorbed form material is a zinc-loaded ion exchange resin, zinc adsorbed on particle surface, composite particles in which zinc salts are incorporated, or mixtures thereof.

In a preferred embodiment, there is a sufficient quantity of zinc ions, such that they would otherwise react with a metallochromic dye zincon to give a dye color change from orange to blue.

A preferred embodiment of the present invention is a method for treating a variety of conditions, including: athlete's foot, microbial infections, improving the appearance of a scalp, treating fungal infections, treating dandruff, treating diaper dermatitis and candidiasis, treating tinea capitis, treating yeast infections, treating onychomycosis. Preferably such conditions are treated by applying a composition of the present invention to the affected area. In a further embodiment of the present invention, a method of treating a condition as described above comprising treating the affected area with a composition comprising a zinc ionophoric material. A further embodiment of the present invention comprises a method of treating a condition as described above comprising treating the affected area with a composition comprising a zinc ionophoric material with a zinc containing material.

A preferred embodiment of the present invention is a method for providing anti-dandruff efficacy comprising applying a ZIM to the hair and scalp.

In a preferred embodiment, the compositions useful in the present invention provide an anti-fungal efficacy.

While particular embodiments of the present invention have been illustrated and described, it would be obvious to those skilled in the art that various other changes and modifications can be made without departing from the spirit and scope of the invention. It is therefore intended to cover in the appended claims all such changes and modifications that are within the scope of this invention.

What is claimed is:

1. A method for delivering excess zinc to eukaryotic cells to inhibit the metabolism of the cell, the method comprising treating the cells with a zinc ionophoric material that is capable of delivering a zinc ion across a cellular membrane wherein the minimum inhibitory concentration (MIC) of the zinc ionophoric material is less than 500 ppm.
2. A method for delivering excess zinc to eukaryotic cells to inhibit the metabolism of the cell, the method comprising treating the cells with a zinc ionophoric material that is capable of delivering a zinc ion across a cellular membrane wherein the zinc ionophoric material is in combination with a zinc containing material and further wherein there is an increase in an intracellular zinc level by 1.5 fold more than would occur in the absence of the zinc ionophoric material preferably an increase in the intracellular zinc level by 2 fold, more preferably an increase in the intracellular zinc level by 2.5 fold.
3. A method according to any of the preceding claims wherein the zinc ionophoric material is present as a zinc salt of the zinc ionophoric material.
4. A method according to any of the preceding claims wherein an increase in zinc transport by 1.5 fold is demonstrated when a zinc ionophoric material is in combination with a zinc containing material to enhance antifungal activity.
5. A method according to any of the preceding claims wherein an increase in a zinc ionophoric material's antifungal activity is achieved with at least a 50% reduction in an amount of zinc ionophoric material necessary to inhibit cell growth when in the presence of 5 ppm or less of a zinc containing material.
6. A method according to any of the preceding claims wherein the zinc containing material reacts with a metallochromic dye zincon to give a dye color change from orange to blue.
7. The method according to any of the preceding claims wherein the zinc ionophoric material is selected from the group consisting of polyvalent metal salts of pyrithiones, preferably wherein the zinc ionophoric material is pyrithione or a zinc salt of pyrithione, more preferably wherein the zinc ionophoric material is zinc pyrithione, dithiocarbamates, preferably wherein the dithiocarbamates are selected from the group consisting of pyrrolidine dithiocarbamate, diethyldithiocarbamate, zinc diethyldithiocarbamate, disulfiram,

dimethyldithiocarbamate, zinc dimethyldithiocarbamate and mixtures thereof, heterocyclic amines, preferably wherein the heterocyclic amines are selected from the group consisting of 8-hydroxyquinoline, 5,7-Diiodo-8-hydroxyquinoline, and 5,7-Dichloro-8-hydroxyquinoline, 5-chloro-7-iodo-8-hydroxyquinoline, chloroquinaldol, 2-methyl-5,7-Dichoro-8-hydroxyquinoline, 5-7-dibromo-8-hydroxyquinoline and mixtures thereof, nonsteriodal anti-inflammatory compounds, naturally occurring materials having zinc ionophoric behavior, and derivatives thereof, bio-molecules and peptides, preferably wherein the bio-molecules and peptides are selected from the group consisting of lasalocid (X537A), A23187 (calcimycin), 4-BR A23187, ionomycin, or cyclosporin A and mixtures thereof, sulfur-based compounds, preferably wherein the sulfur-based compound is tetra-n-butyl thiuram disulfide, transport enhancers, preferably wherein the transport enhancers are selected from the group consisting of albumin, histidine, arachidonic acid, picolinic acid, dihydroxyvitamin D_3, ethylmaltol and mixtures thereof, and mixtures thereof.

8. The method according to any of the preceding claims wherein the zinc containing material selected from the group consisting of inorganic materials, preferably wherein the inorganic material is selected from the group consisting of zinc aluminate, zinc carbonate, zinc oxide, calamine, zinc phosphate, zinc selenide, zinc sulfide, zinc silicates, zinc silicofluoride, zinc borate, or zinc hydroxide and zinc hydroxy sulfate, zinc-containing layered material, and mixtures thereof, more preferably wherein the inorganic material is zinc oxide, natural zinc containing materials, preferably ores, minerals, organic salts, polymeric salts, or physically adsorbed form material and mixtures thereof.

9. The method according to any of the preceding claims wherein the zinc-containing layered material is selected from the group consisting of zinc carbonate hydroxide, zinc copper carbonate, copper zinc carbonate hydroxide phyllosilicate containing zinc ions, layered double hydroxide, hydroxy double salts and mixtures thereof, preferably wherein the zinc-containing layered material is zinc carbonate hydroxide, hydrozincite, basic zinc carbonate and mixtures thereof, more preferably wherein the zinc-containing layered material is hydrozincite.

10. A method of treating microbial infections comprising the use of a composition according to any of the preceding claims.

11. A method of treating fungal infections comprising the use of a composition according to any of the preceding claims.

12. A method of treating dandruff comprising the use of a composition according to any of the preceding claims.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/08476

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/44 A61K33/30 A61P31/02 A61P31/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 00021 A (ARCH CHEM INC) 4 January 2001 (2001-01-04) abstract page 5, line 21 -page 12, line 16 example 2; table 2 tables 4A,4B,6A,6B,8,10A,10B claims 1-3,5,12,13,16,38,42 figures 1,2	1-12
X	US 5 696 169 A (ARIMA YAENO ET AL) 9 December 1997 (1997-12-09) abstract figures 1,2	1-12
Y	column 1, line 55 -column 3, line 35 column 11, line 64 -column 16, line 37; tables 1-12 tables 13-38 claims 1-20	10-12

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search	Date of mailing of the international search report
27 August 2003	09/09/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Felder, C

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/08476

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 00151 A (ARCH CHEM INC ;PROCTER & GAMBLE (US)) 4 January 2001 (2001-01-04) abstract page 3, line 20 -page 3, line 33 page 4, line 16 -page 6, line 19 example 1; table 1 example 2; table 2B examples 3-26 claims 1,5.6,9	1-12
X	GB 2 141 929 A (VICTORIA STATE) 9 January 1985 (1985-01-09) abstract page 1, line 1 -page 1, line 54 tables 3,4 claims 1-28	1-12
X	US 3 236 733 A (KARSTEN KENNETH S ET AL) 22 February 1966 (1966-02-22) column 2, line 14 -column 2, line 48 column 3, line 59 -column 3, line 69 claims 1,5,9	1-12
X	US 5 518 774 A (KAPPOCK PAUL S ET AL) 21 May 1996 (1996-05-21) abstract column 1, line 35 -column 2, line 26 table 1 example 2 claim 1	1-9
Y	the whole document	10-12
X	SAXTON C A ET AL: "ANTIPLAQUE EFFECTS AND MODE OF ACTION OF A COMBINATION OF ZINC CITRATE AND A NONIONIC ANTIMICROBIAL AGENT" SCANDINAVIAN JOURNAL OF DENTAL RESEARCH, COPENHAGEN, DK, vol. 96, no. 3, June 1988 (1988-06), pages 212-217, XP001079620 ISSN: 0029-845X the whole document	1-12

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 10-12 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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